ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

1762. **A Medical Account of the Red River Flood—1950**
G. S. FAHRNI and G. L. M. SMITH. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 331–336, Oct., 1950.

During the period of the Red River flood in 1950 in Winnipeg, Canada, it was necessary to evacuate the civic group of hospitals, involving transport of 1,424 patients and old people. Civil and military medical services combined to deal with the emergency: evacuation by train, air, and ambulance was necessary. The administrative problems, involving close collaboration between military and civil authorities, are fully described.

Scott Thomson

1763. **A Medical Survey in a Gold Coast Village**
M. J. COLBOURNE, G. M. EDINGTON, and M. H. HUGHES. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **44**, 271–290, Dec., 1950. 1 fig., 16 refs.

This is a painstaking, accurate, and complete corroboration of the generally accepted statement that it is normal for Africans to harbour several different parasites, to be relatively undernourished, and to be anaemic.

The village chosen contained 225 inhabitants and was more healthily situated than many; there was no serious poverty, though most of the tenants were in debt to the African landlord. The average height, weight, and blood count were below the standards for Great Britain, and the erythrocyte sedimentation rate was consistently above normal. The spleen rate was 45·5% and the incidence of worm infestation varied from 9·1% for *Schistosoma haematobium* to 75% for *Ascaris lumbricoides*. Hepatomegaly was noted in about one-third and attributed partly to malnutrition, for protein lack seemed evident. About 75% had signs of active or quiescent yaws, and figures are given of the incidence of other diseases.

[The whole picture shows how far the application of scientific knowledge lags behind its acquisition and is a challenge especially to educated Africans.]

Clement Chesterman

1764. **Castor Bean: an Industrial Hazard as a Contaminant of Green Coffee Dust and Used Burlap Bags**
K. D. FIGLEY and F. F. A. RAWLING. *Journal of Allergy* [*J. Allergy*] **21**, 545–553, Nov., 1950. 2 figs., 3 refs.

Nine patients are described who had acquired an allergy to castor bean or castor-bean pomace by contact with jute bags in which these substances had been previously transported. Most of these patients suffered from asthma or rhinitis. Their allergy had at first in most cases been attributed to the dust of green coffee which had been contained in these bags, but later the allergy was traced to castor bean, with which the coffee had been contaminated. Dericinized castor-bean extract is a very potent allergen for man and should not be used for intracutaneous testing, but only for scratch testing.

H. Herxheimer

1765. **The Radiological Appearances in Ochre Pneumoconiosis.** (Über das Röntgenbild der Ockerstaublunge)
R. HAUBRICH. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 682–688, Dec., 1950. 5 figs., 10 refs.

The author describes 8 cases of silicosis of the lungs caused by ochre dust. Radiographs are reproduced showing the appearance of the lung in the second and third stages of the disease. In the second stage the lung field shows fine nodules or a patchy streakiness and resembles the appearance in iron-ore silicosis, and not that seen in the other types of silicosis; the ochre silicosis differs from the iron-ore silicosis, however, in its evolution, which is much slower. The differences between the iron-ore silicosis and the pure iron-dust lung and haemosiderosis (in chronic pulmonary congestion) are pointed out.

A. Orley

1766. **Pulmonary Carcinoma in Chromate Workers. I. A Review of the Literature and Report of Cases**
A. M. BAETJER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 487–504, Nov., 1950. 1 fig., 33 refs.

Some 120 cases (previously published, or known to the author) are surveyed. The material is derived from Germany and the U.S.A. It is indicated that the incidence of carcinoma of the bronchus is related to chromate-producing processes and not to exposure to chromates in other processes.

In one (American) study, 21·8% of all deaths among the chromate-producing workers were ascribed to respiratory cancer, compared with 1·4% in a control group; in another study the figures were 18·2% and 1·2%. A study of all similar plants in Great Britain yielded only one case of respiratory carcinoma. Age distribution, duration of exposure, and time between first exposure and onset of disease are discussed. Age of onset was slightly lower than in the general population, duration of exposure varied widely (4 to 40 years), and the latent

period was similarly variable. Estimations of the degree of intensity of exposure are not available. Clinical features did not differ from those of non-occupational respiratory cancer save in the frequent accompaniment of perforation of the nasal septum (itself a recognized occupational risk). Pathological studies showed that squamous-cell carcinoma was the commonest form. Estimations of chromium content of the tissue gave inconclusive results.

The processes are described. It is stated that the materials used are not radioactive. The mechanism of action of the chromium compound is not known, and animal experiments have not yet been helpful.

L. W. Hale

1767. **Pulmonary Carcinoma in Chromate Workers. II. Incidence on Basis of Hospital Records**
A. M. BAETJER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.* **2**, 505–516, Nov., 1950. 2 refs.

Since 1932 carcinoma of the lung has been scheduled as an occupational disease in the chromate-producing industry in Germany. In 1948 a study in the U.S.A. showed that crude mortality from lung carcinoma was 25 times higher among chromate-producing workers than in a control group.

In the present study distribution by occupation of lung-cancer cases in Baltimore hospitals is compared with that of cases of other diseases in the same hospitals. Methods of selection and analysis are described. The proportion of the former group with an occupational exposure to chromium compounds was significantly higher than among the control group. The percentage of chromate workers in the lung-cancer series was significantly higher than the percentage of chromate workers in the employed male population of Baltimore. The facts submitted confirm the findings of earlier workers that death from lung cancer is more frequent among chromate-producing workers than among the population as a whole. *L. W. Hale*

1768. **Cutaneous Cancer in Relation to Occupation**
S. A. HENRY. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **7**, 425–454, Dec., 1950. 2 figs.

1769. **On Silicosis (Part II).** (Über die Silikose (II Teil))
F. ZOLLINGER, F. LANG, H. R. SCHINZ, U. COCCHI, C. PAGNAMENTA, P. H. ROSSIER, A. BÜHLMANN, J. R. RÜTTNER, A. GLAUSER, H. GESSNER, and H. BÜHLER. *Vierteljahrschrift der Naturforschenden Gesellschaft in Zürich* [*Vjschr. naturf. Ges. Zürich*] Suppl. 2–3, **95**, 1–194, 1950. 62 figs., bibliography.

1770. **Anthracosilicosis in Bituminous Coal Miners. Clinical and Pathological Manifestations**
H. A. SLESINGER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 284–299, Sept., 1950. 6 figs., 8 refs.

1771. **Poliomyelitis in London in 1949**
G. E. BREEN and B. BENJAMIN. *British Medical Journal* [*Brit. med. J.*] **2**, 1473–1475, Dec. 30, 1950. 1 fig., 3 refs.

An account, supported by a spot map and tables, is given of the outbreak of poliomyelitis in the Administrative County of London during 1949, and some comparisons are made with the 1947 outbreak as reported by Daley.

The similarities noted are: (1) A sample of hospital admissions indicates that the percentage of paralytic cases was approximately the same in 1947, 62% of confirmed cases being paralytic and 46% having residual paralysis. The case fatality was 7%, compared with 5% in 1947. (2) The sex ratio was not significantly altered.

Striking dissimilarities were a markedly disproportionate involvement of the London boroughs north of the Thames. In 1947 the spot map gave a general impression of wide scatter, no area escaping. In 1949 it was indeed remarkable that there were wide areas, for example in Deptford and Greenwich, without recorded cases. The slower epidemic rise in 1949 made it possible to discern directions of spread, of which there may have been two main streams: (*a*) from Hampstead, in the north-west, southwards and eastwards, the eastward branch finally turning south to take in a limited area in Deptford and Greenwich; (*b*) from Lewisham, in the south-east, in a north-westward and westward direction.

The most striking observation is the fall in age incidence. Whereas in 1947 only 27·9% of the cases occurred in children under the age of 5, in 1949 the age distribution of cases resembled that seen before 1946, and 53·3% were in children under 5. When the differences between the actual incidence by age groups and the distribution expected on the basis of the 1947 figures is considered, it is found that the largest differences occur in the age group 1 to 2, and the next largest in the group 2 to 4 years. It is suggested that this may perhaps have been due to the earlier outbreak in 1947 raising herd immunity. Unfortunately for this theory the relationship between a high incidence in 1947 in a locality and a lowering of the average age incidence in the same locality during 1949 is not a simple one. This difficulty is discussed.

The 1949 outbreak showed a more leisurely development both in time and in space than the 1947 epidemic.

W. H. Bradley

1772. **The Epidemiology of Psittacosis in the Argentine.** (Epidemiologia de la psitacosis en la Republica Argentina)
H. R. RUGIERO, S. AVERBACH, M. CARLONE, and J. LANDABURU. *Prensa Médica Argentina* [*Prensa méd. argent.*] **37**, 2593–2599, Oct. 27, 1950. 40 refs.

1773. **Medical Investigations in North Greenland 1948–1949. V. Rheumatic Diseases. Comparative Investigations regarding their Incidence.** (Internmedicinska undersökningar pä Nord-Grönland 1948–1949. V. Reumatiska sjukdomar jämförande frekvensundersökning)
M. C. EHRSTRÖM. *Nordisk Medicin* [*Nord. Med.*] **44**, 1787–1789, Nov. 10, 1950. 2 figs., 1 ref.

Anatomy and Cytology

1774. **The "Clear" Ciliated Epithelial Cells of the Mucous Membrane of the Human Uterus.** (Über die "hellen" Flimmerepithelzellen der menschlichen Uterusschleimhaut)

H. HAMPERL. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **319**, 265–281, 1950. 12 figs., 26 refs.

Morphological details of the life-cycle of ciliated epithelia in polypi and hyperplasia of the uterine fundus have been studied at the Institute of Pathology of Marburg University. Tissue obtained at operation was fixed in formalin and the frozen sections were immediately transferred to a slide on which they were stained by metachromizing thionine; the cilia were demonstrated by staining with *ponceau de xylidine*.

Interspersed among the narrow columnar cells of the endometrium were found clear, broad cells with large nuclei, arranged singly, in small groups, or in sheets. These clear cells were bulbous and tapered somewhat towards the base and the free surface; they appeared to push aside the adjoining darker, non-ciliated cells. Within these clear cells a "ciliary vesicle" formed which moved towards the free edge of the cell, broke open, and displayed the cilia which now formed a fringe all over the free surface of the cell; this fringe might be discharged from the cell by apocrine secretion in the form of a globule bearing cilia all over its surface. Evidence is adduced that all ciliated cells of the hyperplastic endometrium are "clear" cells. But not all clear cells are ciliated; these cells are of three types, namely: (1) ciliated, (2) migrating lymphocytes, (3) special non-ciliated clear cells.

[This paper is illustrated by very clear and convincing photomicrographs (magnification × 1600).]

N. Alders

1775. **The Effect of Oxygen Lack on Development of the Mammalian Foetus.** (Untersuchungen über den Einfluss des Sauerstoffmangels auf die fötale Entwicklung von Säugetieren)

A. WERTHEMANN, M. REINIGER, and H. THOELEN. *Schweizerische Zeitschrift für Allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path.*] **13**, 756–779, 1950. Bibliography.

The effects of oxygen lack on mammalian foetal development were studied in (*a*) pregnant rabbits subjected to constriction of the uterine artery on one side, and (*b*) pregnant rats subjected to low atmospheric pressures. The rabbits were mostly operated on 2 to 3 days after mating, and the uterus and adnexa were removed 10 to 29 days after mating. A total of 68 embryos were obtained from 10 rabbits, 33 from the operated side and 35 from the intact side. Of these, 34 from the intact side were normal, but only 23 from the operated side. Absorption of the embryo occurred only once on the intact side, but 10 times on the operated side. Of 13 embryos investigated microscopically, several showed brain abnormalities such as hydrocephalus, haematocephalus, and maldevelopment of the mid-brain.

In the experiments on rats 24 pregnant animals were studied. These were fed on a standard diet and then kept for 48 hours in a pneumatic chamber. One group was kept at a pressure of 760 mm. Hg, another at 460 mm., and a third at 360 mm. The average size of litter was less in the last 2 groups, being only about half the normal at 360 mm. Only 6% of the normal group were stillborn, whereas the 460-mm. group contained 33% of stillbirths and the 360-mm. group 15%. Reabsorption of embryos was much more frequent than normal in the low-pressure groups, being over 40% at 360 mm. The length and weight of the surviving offspring were slightly above average, and the period of gestation was increased by about 2 days at reduced pressure. It is suggested that low oxygen tension causes a disturbance of endocrine function resulting in faulty development of the placenta.

R. Barer

1776. **Observations on the Distribution of Subcutaneous Fat**

D. A. W. EDWARDS. *Clinical Science* [*Clin. Sci.*] **9**, 259–270, 1950. 5 figs., 1 ref.

The thickness of a fold of skin and subcutaneous tissue was measured in 53 selected regions of the body with a pair of engineer's vernier callipers, modified by building up the jaw face to avoid indentation, on 83 nulliparous and 55 parous women, and also on 24 women who were taking a reducing diet and were losing weight. None of the subjects was suffering from endocrine or wasting diseases. Their height and weight were also recorded, and the latter corrected to a value corresponding to a standard height of 64 inches (1·62 m.).

A series of graphs and tables is presented showing the relation between the body weight and the estimate of the total subcutaneous fat (based on the sum of all 53 readings on a subject), and also that between body weight and the thickness of the subcutaneous tissue at different sites. A correction was made for the double skin thickness included in the fold, the thickness having been measured at each site in 8 female cadavers.

There was found to be a close relationship between body weight and total subcutaneous-tissue thickness, both in the group figures and those for the individual patients who were losing weight. The thickness at different sites was found to vary according to a constant pattern which included a relatively greater deposition of fat around the shoulders, back, abdomen, and thighs, with a sparing of the extremities. Some common variations of the normal distribution are also described.

D. B. Moffat

Physiology and Biochemistry

1777. **The Measurement of Total Body Water in the Human Subject by Deuterium Oxide Dilution. With a Consideration of the Dynamics of Deuterium Distribution**
P. R. SCHLOERB, B. J. FRIIS-HANSEN, I. S. EDELMAN, A. K. SOLOMON, and F. D. MOORE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1296–1310, Oct., 1950. 8 figs., 49 refs.

At the Peter Bent Brigham Hospital and Harvard Medical School, Boston, Massachusetts, the authors measured total body water in 17 normal adult men and 11 normal adult women by means of a technique for determining the dilution of intravenously injected deuterium oxide. [The paper and the references given therein should be consulted for details of the complicated analytical technique.] In the men the mean total body water was 44·2±2·3 litres or 61·8±3·5% of body weight, while in women the mean was 30·0±3·1 litres or 51·9±4·7% body weight. On the whole these results compare satisfactorily with those of others using the same or different methods. Total body water correlated most closely with surface area and oxygen consumption at rest in the individuals studied. There were marked variations in total body water per litre of plasma volume in the small number of subjects studied, and very poor correlation with extracellular fluid volume measured as thiocyanate space. The deuterium oxide concentration attained in the serum in these experiments was about 0·2 volumes %, which is well below the toxic level. Deuterium oxide equilibrated with body water within 2 hours of intravenous injection. After oral ingestion or subcutaneous injection equilibration occurred in 3 hours. In 2 subjects the deuterium oxide concentration in the gastric secretion was studied and was found to be higher than that in venous blood, both samples being taken simultaneously 10 minutes after intravenous injection. Analysis of simultaneous samples of blood and urine showed identical concentration after equilibrium had been reached. Deuterium was excreted into the urine at the rate of 0·1% of the administered amount per hour. From the investigation of the disappearance of deuterium oxide from the body over a period of 40 days it is calculated that 7·7±1·2% total body water is replaced daily. The half-life of deuterium oxide in the body of the human adult is 9·3±1·5 days. *Walter H. H. Merivale*

1778. **Effects of 17-Hydroxy-corticosterone (" Compound F ") in Man**
P. FOURMAN, F. C. BARTTER, F. ALBRIGHT, E. DEMPSEY, E. CARROLL, and J. ALEXANDER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1462–1473, Nov., 1950. 8 figs., 18 refs.

Work with adrenocorticotrophic hormone (ACTH) has suggested that the adrenal cortex produces three types of hormone, one affecting carbohydrate metabolism (" sugar " or " S " hormone), one affecting Na and K metabolism (" Na " hormone), and one with somatotrophic and androgenic properties (" nitrogen " or " androgenic " hormone). Earlier work by the present authors indicated a possibility that " S " hormone could influence K balance and hence Na balance, so that the postulation of a separate " Na " hormone in response to ACTH stimulation is unnecessary. This paper describes the investigation of this possibility by the use of a pure " S "-hormone-like substance, 17-hydroxycorticosterone or compound F.

Compound F (50 mg.) was administered to a normal man in four doses on each of two separate days, and its effects were studied on the ensuing three days as compared with three corresponding control days, the diet being identical on all the days. The urinary excretion of nitrogen, potassium, sodium, chloride, phosphorus, calcium, magnesium, and 17-ketosteroids was determined, and also the blood sugar and eosinophil levels. Glycosuria occurred after compound F on both occasions, but without a raised blood sugar level, indicating a lowered renal threshold. A fall in eosinophil count followed the injections and there was a slight loss of nitrogen, as expected. The effect on the excretion of K was more marked than on any of the other electrolytes: K loss began soon after injection, and 20 mEq. was lost before large dietary intake restored the balance. Some water and salt retention occurred, but the observations were difficult to interpret. Changes in phosphorus, calcium, and magnesium output were not significant: 17-ketosteroid excretion was slightly reduced.

The authors conclude that since compound F, with " S "-hormone-like action, reproduces the changes in K, Na, and Cl balance characteristic of ACTH, there is no need to postulate that a separate " Na " hormone is secreted when the adrenals are stimulated by ACTH.
Nancy Gough

1779. **The *in vitro* Production of Cortisone by Mammalian Cells**
H. SENECA, E. ELLENBOGEN, E. HENDERSON, A. COLLINS, and J. ROCKENBACH. *Science* [*Science*] **112**, 524–525, Nov. 3, 1950. 6 refs.

Adrenal tissue was incubated at 37° C. in a complex nutrient medium with deoxycortone, and the formation of corticosterone determined by extraction and examination by paper chromatography. The addition of vitamins C, B_1, B_2, and B_6, nicotinic acid, and insulin gave the best results, omission of any or all of these materials giving lower yields of cortisone. Addition of glutathione to this optimum medium gave completely negative results. The highest positive results were given by the adrenals of the cat and man (one case) followed by the dog, rat, and guinea-pig, those of the chicken being negative. Liver, testis, kidney, and ovary gave a few positive results. *F. W. Chattaway*

1780. **Physiological Effects and Possible Methods of Reducing the Symptoms Produced by Rapid Changes in the Speed and Direction of Airplanes as Measured in Actual Flight**

J. R. POPPEN and C. K. DRINKER. *Journal of Applied Physiology* [*J. appl. Physiol.*) 3, 204–215, Nov. 1, 1950. 8 figs.

The results of experiments carried out in 1932–34 are reported. Dogs anaesthetized with pentobarbitone were mounted in aircraft in a position similar to that of the pilot and subjected to rapid horizontal turns and to dives. The carotid arterial, jugular, and femoral venous and arterial pressures were recorded directly during the manœuvres. The carotid pressure fell to an extent proportional to the severity and duration of the acceleration. There was an immediate sharp rise in the femoral venous pressure. It was concluded that "blackout" is caused by severe cerebral anoxaemia due to sudden reduction in the intracranial circulation. It was shown that by fitting a belt containing an inflatable bag around the abdomen of the dog and raising the intra-abdominal pressure by inflation of the belt shortly before or during the acceleration the fall in carotid pressure could be greatly reduced. *D. H. Sproull*

CIRCULATORY SYSTEM

1781 (*a*). **Variations in the Duration of Phases of the Cardiac Cycle in Normal Hearts as Studied by the Electrokymograph**

K. WILLIS, E. E. EDDLEMAN, J. K. ACKER, E. POULOS, and H. E. HEYER. *American Heart Journal* [*Amer. Heart J.*] **40**, 485–503, Oct., 1950. 11 figs., 22 refs.

The phases of the cardiac cycle in 60 healthy subjects have been analysed by means of electrokymography, the apparatus used being equipped for the simultaneous recording of the electrokymographic tracing, heart sounds, and carotid sphygmogram. The authors used a standardized technique on all the subjects and obtained electrokymographic tracings of the cardiac cycle in which the following phases could be detected: (1) Systolic phases: isometric contraction, rapid ejection, reduced ejection, total ejection. (2) Diastolic phases: protodiastole plus isometric relaxation, rapid filling, diastasis, and total diastole. The mean duration of cycle and its systolic and diastolic phases and the range of values obtained are listed in a table. Emphasis was placed upon the analysis of the aortic knob and left ventricular border tracings. In another table the duration of the various cardiac phases in normal human subjects as determined by other methods are compared with the values found by electrokymography.

The factors which were considered to alter the duration of some of these phases were alteration in heart rate, change of posture (see Abstract 1781 (*b*)), increased venous return, and change in peripheral resistance. Graphs plotting the duration of the various phases of the cardiac cycle against the total cycle length revealed that there was "an apparent direct correlation of cycle length with the phases of reduced ejection, total systole, reduced filling, and total diastole. There was a questionable correlation of rapid filling to cycle length. There was no direct correlation of cycle length to the phases of isometric contraction, rapid ejection, protodiastole, and isometric relaxation."

[This paper should be read in the original by those interested in the application of electrokymography to cardiology.] *A. I. Suchett-Kaye*

1781 (*b*). **The Effect of Posture on the Cardiac Cycle, Postero-anterior Cardiac Diameters, and Apparent Stroke Volume as Studied by the Electrokymograph**

E. E. EDDLEMAN, K. WILLIS, and H. E. HEYER. *American Heart Journal* [*Amer. Heart. J.*] **40**, 504–521, Oct., 1950. 7 figs., 15 refs.

This communication deals with the effects of change from the recumbent posture to the vertical position on (1) the cardiac cycle, (2) postero-anterior cardiac diameter, and (3) apparent stroke volume, as studied by electrokymography. The subjects of the experiment were young, healthy, male medical students, and the following results are reported: (1) As regards the systolic phases of the cardiac cycle, no significant change was observed in the duration of isometric contraction, but there was shortening of the other phases (rapid ejection, reduced ejection, total ejection) and of total systole. The effect on the diastolic phases was to increase the duration of protodiastole plus isometric relaxation, and also to increase the duration of the rapid-filling phase. The cycle length as a whole was appreciably shortened on assuming the standing position, the mean duration for the lying position being found to be 1·054 second, and for the standing position only 0·75 second. (2) As regards the postero-anterior diameter of the heart, in 9 of 10 subjects an increase was noted in the diastolic and systolic diameter when the upright posture was assumed. (3) The apparent stroke volume decreased by an average of 38% on standing up.

The authors also describe the effect of venous compression and venesection on the phases of the cardiac cycle. In an appendix is described the method for the determination of the postero-anterior cardiac diameters and apparent stroke volumes on the electrokymographic principle. *A. I. Suchett-Kaye*

1782. **Excitability of the Mammalian Ventricle throughout the Cardiac Cycle**

O. ORIAS, C. M. BROOKS, E. E. SUCKLING, J. L. GILBERT, and A. A. SIEBENS. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 272–282, Nov. 1, 1950. 5 figs., 29 refs.

By improved methods of investigation it has been shown that in the heart of the dog asymmetrical recovery of excitability occurs during the relative refractory period. The threshold strength of stimuli of varying duration applied to the ventricle was determined at various points throughout an artificially induced cycle. It was found that recovery of excitability during the relative refractory period was not a symmetrical, smoothly progressive process, but included periods of relatively

increased excitability, demonstrated by the presence of " dips " in the curve relating threshold intensity of the stimulus to the time of its application during the cycle. Curves for stimuli of long duration revealed one major dip at 150 milliseconds and one, or rarely two, occurring at 120 to 150 milliseconds. Curves for stimuli of different duration showed these dips at the same position in the cardiac cycle except when there was some change in the condition of the heart which modified the duration of refractoriness. Not only were there oscillations or asymmetry in the process of recovery of excitability, there were also changes in sensitivity to different forms of stimulation, such as those applied with anodal as opposed to cathodal stigmatic electrodes. Evidence is presented suggesting that there are intervals of the cycle during which the heart cannot respond to excitatory processes, but that there are no intervals during which an excitatory process cannot be produced in cardiac muscle. Practically no evidence of supernormality of the ventricle was found, and it is suggested that supernormality might merely be a continuation into the early phase of the post-refractory period of the oscillations in excitability threshold found during the relative refractory period.

William A. R. Thomson

1783. **Plasma and Blood Volumes of Mouse Organs, as Determined with Radioactive Iodoproteins**

N. KALISS and D. PRESSMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 16–20, Oct., 1950. 15 refs.

The authors have used three different preparations of radio-iodinated protein, a globulin fraction of rabbit anti-ovalbumin serum and two bovine serum-albumin preparations. A dose of the radioactive preparation containing about 0·5 μc. of ^{131}I was injected intravenously into 6- to 7-week-old male mice (17 to 25 g.) and allowed to circulate for periods ranging from 15 minutes to over 1 hour. Total plasma volume was calculated by determining the radioactivity of a measured volume of the peripheral blood. To determine the volume of the individual organs, the mice were killed and the organs ligated, excised, weighed, and homogenized and their radioactivity appraised. The average plasma and blood volumes of the mouse were 6·7 and 12·7 ml. per 100 g. respectively. The average plasma volume, in ml. per 100 g. wet tissue, of the brain was 1·6; kidney, 19·1; liver, 20·2; lung, 23·9; small intestine, 5·0; spleen, 9·2; submaxillary gland, 5·9; and testis, 3·4.

Malcolm Woodbine

1784. **The Mechanism of Clot Retraction**

A. J. QUICK and C. V. HUSSEY. *Science* [*Science*] **112**, 558–559, Nov. 10, 1950. 2 figs., 7 refs.

It is known that clot retraction requires the presence of intact platelets, and that the extent of retraction is quantitatively dependent on the number of platelets. In the present experiments only three agents were used, namely, washed fresh platelets in suspension, purified fibrinogen, and thrombin. With a constant fibrinogen concentration and constant number of platelets the extent of retraction depends directly on the thrombin concentration, being absent with very small concentrations and reaching a fixed maximum at a thrombin concentration which depends on the amount of fibrinogen present. When the concentration of thrombin and the number of platelets is constant there is an inverse (but not linear) relationship between clot retraction and fibrinogen concentration. With a fibrinogen concentration of 0·25% (the average level in normal plasma) there is almost no retraction; retraction is maximal with a fibrinogen concentration of 0·05%.

P. Mestitz

1785. **Morphology and Enumeration of Human Blood Platelets**

G. BRECHER and E. P. CRONKITE. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 365–377, Dec., 1950. 1 fig., 18 refs.

The effect of various anticoagulants was observed on the platelet count and platelet morphology in 50 normal males at the United States Naval Research Station. The authors advise using 1% ammonium oxalate as a diluting fluid to destroy the erythrocytes, collecting the blood by venepuncture with a siliconed syringe, and counting with a phase-contrast microscope. They found no significant loss of platelets when the diluted specimen was stored at 5° C. for 3 days. The authors made 5 successive daily counts on 10 normal subjects and found that there was a greater variation between individuals than in the same person from day to day.

The reproducibility of platelet counts is discussed in relation to Berkson's equation of the expected total error. The authors agree that accuracy is increased by increasing the number of pipettes and counting chambers used, rather than by counting more cells.

Ernest T. Ruston

1786. **The Influence of Liver Extract and Vitamin B_{12} on the Production of Erythrocytes *in vitro*.** [In English]

J. D. MAGNUSSEN. *Acta Pharmacologica et Toxicologica* [*Acta pharmacol., Kbh.*] **6**, 263–268, 1950. 2 figs., 4 refs.

The author has shown that crystalline vitamin B_{12}, added to the fluid in which bone-marrow cells are suspended, can replace liver extract as the essential substance for development of erythrocytes *in vitro*. The experiments were carried out with rabbit bone marrow suspended in Ringer's solution with 30% rabbit serum, to which was added the liver extract or the vitamin B_{12}. The erythrocytes were counted at the start of the experiment and after 5 hours at 37° C.; the number of erythrocytes formed per erythroblast was also calculated.

Malcolm Woodbine

1787. **The Adrenal Gland and Hemopoiesis**

S. J. PILIERO, D. LANDAU, and A. S. GORDON. *Science* [*Science*] **112**, 559–560, Nov. 10, 1950. 12 refs.

Experiments were carried out in which adult female rats were observed for periods up to 8 weeks after adrenalectomy, the animals being maintained on 1% sodium chloride in the drinking water; an anaemia developed, reaching its peak (20 to 25% below normal) within 2 to 3 weeks after operation, associated with a decreased

erythrocyte fragility. The erythrocyte values tended to rise towards normal after 3 weeks, but they had not reached it within 8 weeks. There was no change in the total and differential leucocyte counts. In the bone marrow of adrenalectomized rats 2 weeks after operation there was a rise in the proportion of all myeloid components present and a fall in that of nucleated erythroid elements. Administration of whole adrenal cortical extract prevented the change in the erythrocyte count, but had no effect on the marrow myeloid elements. Cortisone acetate (0·5 to 1·0 mg. per day) was partly effective in restoring the myelogram to normal. It also decreased the peripheral eosinophil count in adrenalectomized animals. Adequate controls were carried out at all stages of the work. *P. Mestitz*

NUTRITION AND DIGESTION

1788. **Motility Studies of the Cardia and Oesophagus.** (Motilitätsstudien an Kardia und Ösophagus)
H. BARTELHEIMER and H. JANSSON. *Deutches Archiv für Klinische Medizin.* [*Dtsch. Arch. klin. Med.*] **197**, 578–588, 1950. 7 figs., 11 refs.

Oesophageal motility was studied by means of a thin rubber balloon filled with water and connected by tubing of 4 mm. diameter to a glass capillary tube, in which the height of the water column was recorded photographically. It was found that the form of the oesophageal contractions was most easily seen if the sensitized paper was set to move at 6·5 cm. per minute.

Normal peristalsis was defined as having a period of 24 to 120 seconds between contraction peaks [though even with this wide range only 7 out of 11 symptom-free subjects were classified as normal]. Patients with gastro-intestinal disease and deficiency syndromes were investigated, but no consistent abnormality of oesophageal motility was found.

[Distension of the oesophagus by a stationary object is unphysiological, and the resulting motility-response depends on a number of factors which are not mentioned in this paper.] *Denys Jennings*

1789. **Studies on the Stimulation Mechanism of Gastric Secretion.** [In English]
S. LINDE. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] Suppl. 74, **21**, 1–92, 1950. 30 figs., bibliography.

1790. **Iron Metabolism. The Pathophysiology of Iron Storage**
C. A. FINCH, M. HEGSTED, T. D. KINNEY, E. D. THOMAS, C. E. RATH, D. HASKINS, S. FINCH, and R. G. FLUHARTY. *Blood* (*Blood*] **5**, 983–1008, Nov., 1950. 5 figs., bibliography.

In this paper from the Peter Bent Brigham Hospital, Boston, Massachusetts, the authors discuss normal and abnormal iron metabolism and describe experiments carried out on animals to elucidate questions of iron storage and utilization. The distribution and availability of stored iron were studied in dogs, the degree of localization of stored iron in rats, and changes in total body content of iron under various conditions in mice. In addition the organs of patients with haemochromatosis were analysed post mortem for iron content.

Storage iron—the iron which can be mobilized from the body tissues for the formation of haemoglobin—is present intracellularly in the form of two similar compounds, ferritin and haemosiderin. The body of a normal man contains about 5,000 mg. of iron, of which storage iron constitutes 20%. As only a fraction of a milligramme is excreted daily in the urine and faeces, excess iron must be stored and is found in the reticulo-endothelial or parenchymal cells, the liver being the most important organ involved. In iron deficiency anaemia the absorption of iron is increased, but the iron is used directly for haemoglobin synthesis and is not stored. The iron stores thus remain depleted for a period which may extend over many months.

The authors state that increased absorption and storage of iron may be produced in animals by altering the composition of the diet. In such cases there is an increase in the serum and liver iron content and eventually haemosiderosis develops. The distribution of iron is similar to that seen in cases of haemochromatosis. In animals given intravenous injections of iron-ascorbate gelatin and observed for periods up to 2 years massive deposits of iron were found in the reticulo-endothelial system, whereas excess iron given by mouth or injected in small quantities in the form of soluble salts was stored predominantly in the liver. When erythrocytes labelled with radioactive iron were injected into rats, it was found that the spleen absorbed most of the erythrocytes, whereas haemoglobin injected in solution was mostly concentrated in the kidneys. Iron localization after the breakdown of blood thus depends on whether the breakdown is intravascular or extravascular. Focal deposits of iron in various organs such as the brain, lungs, and skin indicate previous breakdown of blood in the areas involved. The serum iron level, although always low in the presence of infection, is a measure of excess iron storage, while the amount of stored iron may also be determined by examination of the liver or bone marrow. No evidence was found that the stored iron in haemochromatosis differs from that stored when iron is injected. In dietary or idiopathic haemochromatosis there is an excess absorption of iron, and it is stated that by giving large doses of iron and a diet of low phosphate content an increase in body iron storage may be produced. *T. M. Pollock*

1791. **Peptide Wastage Consequent to the Infusion of Two Protein Hydrolysates**
H. N. CHRISTENSEN. *Journal of Nutrition* [*J. Nutrit.*] **42**, 189–193, Oct. 10, 1950. 4 refs.

Protein hydrolysates were administered intravenously to 6 normal subjects, the preparations used being: (1) fibrin hydrolysed by acid until it was practically peptide-free, so that only 4% of the amino-acids remained in the bound form; and (2) bovine plasma hydrolysed by pancreatic enzymes, in which 47% of the amino-acids

remained in the bound form. Urine and blood samples were taken during the period of infusion and the next 4 hours and their peptide content determined. After infusion of the former hydrolysate there was a minimum urinary wastage of peptides, this being approximately one-third of the small amount of peptide administered; peptides were not found in the plasma at the end of the infusion or within 1½ hours subsequently. After infusion of the peptide-rich hydrolysate there was urinary wastage of 31% of the administered peptides; there was marked plasma peptidaemia, the plasma peptide level at the end of the infusion being as high as 9·2 mg. per 100 ml. The amounts of free amino-acids contained in the hydrolysates were 5·17 g. and 3·23 g. per litre respectively; the urinary wastage of free amino-acids was between 4% and 6% with the former, and between 4% and 8% with the latter. It is clear, therefore, that there was greater retention of the former hydrolysate.

Joseph Parness

1792. **Minimal Sodium Losses through the Skin**
K. D. ARN and A. REIMER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1342–1346, Oct., 1950. 14 refs.

1793. **Effect of Cooking Methods on Retention of Vitamins and Minerals in Vegetables**
W. A. KREHL and R. W. WINTERS. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **26**, 966–972, Dec., 1950. 11 refs.

Four methods of cooking were compared for their effects on the retention of minerals and vitamins in twelve common vegetables, which included cabbage, potatoes, peas, and beans. The minerals studied were calcium, iron, and phosphorus, and the vitamins were carotene, riboflavin, nicotinic acid, aneurin, and ascorbic acid. The methods of cooking were: (1) boiling in water just covering the vegetables; (2) boiling in a small amount of water [roughly the conditions advocated by the Ministry of Food as the " conservative " method]; (3) pressure cooking at 15 lb. per sq. inch (1·05 kg. per sq. cm.); (4) cooking in a new type of " waterless cooker ". On the whole, the minerals were retained better than the vitamins (60 to 100% retention compared with 40 to 100%). The retention of both minerals and vitamins was inversely proportional to the amount of water used, so that it was best with the waterless cooker, not quite so good with the pressure cooker, worse with the conservative saucepan method, and worst with the saucepan containing larger amounts of water. *J. Yudkin*

1794. **Vitamin Studies in Middle-aged and Old Individuals. V. Hypovitaminemia B_1. Effect of Thiamine Concentration and Clinical Signs and Symptoms**
M. CHIEFFI and J. E. KIRK. *Journal of Gerontology* [*J. Gerontol.*] **5**, 326–330, Oct., 1950. 3 figs., 4 refs.

To 20 patients aged 54 to 101 years (average 74 years) in whom the blood aneurin level was less than 2 μg. per 100 ml., 5 mg. of aneurin hydrochloride was given daily by mouth for 15 weeks. The patients were observed during treatment and for 6 months afterwards The blood aneurin level reached normal within 2 weeks of the start of treatment, but fell to below normal after 6 months. Of 15 patients with oedema of the legs, 13 were relieved by treatment, but 8 of these 13 had relapsed at the end of the 6-month period. Relief was obtained by 4 patients with tenderness of the calves after 3 weeks' treatment, but the symptom returned in 3 after 6 months. Of 5 patients with impaired vibration sense in the legs, 4 regained normal sensation on treatment; one of these had relapsed after 6 months. Only 2 of 12 patients with subconjunctival thickening improved with treatment; neither of these relapsed after aneurin administration was discontinued. Of 3 patients with fissures of the tongue, 2 were relieved by treatment, but in both there was a relapse when treatment was stopped. Redness of the tongue, which was seen in 5 patients, disappeared after 10 weeks' treatment, but returned after 6 months. In all 20 patients there was an increase in appetite, but weight gain averaged only 2 kg.

It was concluded that aneurin deficiency was responsible for the oedema of the legs, tenderness of the calves, and redness of the tongue in these patients.

P. D. Bedford

1795. **Experimental Studies on Calciferol Poisoning. Behaviour of Serum and Organ Calcium in Dogs Poisoned with Calciferol.** (Experimentelle Untersuchungen zur Vitamin-D2-Vergiftung. Das Verhalten des Serum- und Organcalciums bei vitamin-D2-vergifteten Hunden)
G. SCHETTLER and M. SCHÖNINGER. *Zeitschrift für die Gesamte Experimentelle Medizin* [*Z. ges. exp. Med.*] **116**, 423–430, 1950. 16 refs.

Calciferol, in doses of from 4 to 20 mg. per kg. body weight, was given to dogs by mouth, intramuscularly, or intraperitoneally. A single dose increased the calcium content of kidney, lung, spleen, heart, and aorta, as well as the serum calcium concentration. The rise in calcium content began very soon (within 24 hours in the case of the kidney and serum) after the administration of calciferol. Kidney and lung showed the biggest increases in calcium content; no constant increase in liver calcium could be found. The raised calcium content of the organs was not due merely to the high calcium concentration in the blood (and urine in the case of the kidney) still present in these organs on analysis. In surviving animals the amounts of calcium in the organs and in the serum gradually fell. However, in one animal killed on the 112th day after a single dose of calciferol (5 mg. per kg.), when all signs of calciferol intoxication had disappeared, the calcium content of the kidney was still raised. Other findings confirmed that the calcium content of organs may be still raised after all toxic symptoms have vanished. No correlation could be established between the severity of the intoxication and the calcium content of the organs and the serum. *P. Mestitz*

1796. **Effect of Hypervitaminosis A on Foetal Mouse Bones Cultivated *in vitro*. Preliminary Communication**
H. B. FELL and E. MELLANBY. *British Medical Journal* [*Brit. med. J.*] **2**, 535–539, Sept. 2, 1950. 6 figs., 16 refs.

Pharmacology and Therapeutics

1797. **Actions and Clinical Assessment of Drugs which Produce Neuromuscular Block**
W. D. M. PATON and E. J. ZAIMIS. *Lancet* [*Lancet*] **2**, 568–570, Nov. 18, 1950. 2 figs., 13 refs.

The fundamental action of decamethonium on skeletal muscle is depolarization of the muscle membrane at the motor end-plate. The first effect of this, especially when the drug is injected into a muscle by an arterial route, is to excite a brief contraction. The depolarization then persists and spreads to adjacent regions of the muscle. Since the end-plate is already partly depolarized, a nerve impulse can no longer evoke so large an end-plate potential. The surrounding muscle also becomes depolarized with the result that it is electrically inexcitable. The effect is similar to that produced when acetylcholine is caused to persist by giving anticholinesterases, and decamethonium may be regarded as acetylcholine which cannot be hydrolysed. In contrast, D-tubocurarine cannot depolarize muscle, and its action depends on preventing acetylcholine from doing this. The mechanisms of action of these two drugs are therefore diametrically opposed and this is confirmed by the fact that D-tubocurarine can antagonize the effects of decamethonium.

Many differences occur between the two drugs which must be borne in mind when using techniques of neuromuscular block which have been evolved with D-tubocurarine. Muscles differ in their sensitivity to both drugs, but these differences are not the same in each case. For example, with D-tubocurarine the soleus is more easily paralysed than the tibealis in the cat, while with decamethonium the tibealis is paralysed first. Species also vary in their sensitivity to the two drugs. Ether anaesthesia slightly potentiates D-tubocurarine, but slightly antagonizes decamethonium. Adrenaline potentiates the stimulant action of decamethonium. It also changes the relative potency of D-tubocurarine and decamethonium. It also changes the relative potency of D-tubocurarine and decamethonium on a given muscle. For example, intravenous adrenaline lessens the maximum effect of decamethonium on the tibialis from 95 to 78% paralysis, while it increases that of D-tubocurarine on the tibialis from 60 to 75%. Adrenaline also changes the pattern of muscle susceptibility to the drugs in opposite ways, increasing the effect of decamethonium on the soleus and decreasing that of D-tubocurarine on the soleus. The most important practical consequence of differences between the mode of action of the two drugs is that a comparison of their clinical usefulness can only be made under the conditions of actual use. If it is necessary to find out which of the two drugs has the greater or lesser effect on a muscle, the comparison must be made on the actual muscle in the actual species. Failure to observe this has invalidated some recent work.

[A consequence of this paper, which is of fundamental importance to anyone working with these drugs, is that the term "muscular relaxant" or "neuromuscular blocking agent" should be substituted for "curarizing agent" in referring to decamethonium.] *R. Hodgkinson*

1798. **Evaluation of Curarizing Drugs in Man. V. Antagonism to Curarizing Effects of D-Tubocurarine by Neostigmine, *m*-Hydroxy Phenyltrimethylammonium and *m*-Hydroxy Phenylethyldimethylammonium**
D. W. MACFARLANE, E. W. PELIKAN, and K. R. UNNA. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 382–392, Nov., 1950. 3 figs., 20 refs.

1799. **The Effect of 2:2-Diethyl-1:3-propanediol (a New Anticonvulsant) on Spinal Cord Reflexes**
I. H. SLATER, J. F. O'LEARY, and D. E. LEARY. *Journal of Pharmacology and Experimental Therapeutics* [*J. pharmacol.*] **100**, 316–324, Nov., 1950. 3 figs., 11 refs.

In spinal cats or cats under "diol" and "methone", 2 : 2-diethyl-1 : 3-propanediol given intravenously in doses of 12·5 to 50 mg. per kg. abolishes the flexion reflex recorded from the anterior tibial muscle, but does not affect the knee-jerk. In those animals which show a crossed extension reflex this also is abolished. In anaesthetized cats it causes a fall of blood pressure and may stop respiration, which can be restored by leptazol. It is effective as an antagonist to leptazol, strychnine, or electric convulsions. *V. J. Woolley*

1800. **Relation of Hyaluronidase to Salicylates and Rheumatic Fever**
A. A. JAWORSKI, J. E. FARLEY, J. BARRETT, and R. A. JAWORSKI. *Journal of Pediatrics* [*J. Pediat.*] **37**, 697–708, Nov., 1950. 2 figs., 36 refs.

Working in Pawtucket, U.S.A., the authors have investigated the effects of salicylate and succinate on hyaluronidase activity in normal and rheumatic subjects (4 showing signs of active disease and 18 convalescent from acute rheumatism). As controls they used 22 children recovered from primary tuberculosis. The hyaluronidase was a highly purified extract of bovine testicular origin which produced no inflammation on injection. The indicator dye used was Evans blue (T—1824). The authors made many comparisons between the spreading of the dye in rheumatic and non-rheumatic subjects with and without salicylate and succinate therapy. The area of dye spread with hyaluronidase was significantly greater in rheumatic than control subjects, thus confirming the findings of previous workers in this field. A most important finding was that in rheumatic subjects salicylate therapy had no inhibiting effect on the spreading of the dye whether hyaluronidase was injected simultaneously or not. In the non-rheumatic subjects, however, oral administration of salicylate to produce a

blood level of 18·5 mg. per 100 ml. brought about a 30·4% decrease of dye spread with hyaluronidase, and a 17·8% decrease without hyaluronidase injection. Hyaluronidase is an enzyme which can be extracted not only from many tissues, but from a variety of organisms, including the streptococcus, which is closely associated with rheumatic fever. The authors suggest that increased allergy to hyaluronidase may explain why some subjects develop acute rheumatism in the presence of a streptococcal infection while others do not. The significance of the observation that salicylates inhibit hyaluronidase effects in normal and not in rheumatic subjects remains undetermined. *William Hughes*

1801. **The Effect of Water-soluble Preparations of Vitamin K in Dicumarol-induced Hypoprothrombinemia**
S. SHAPIRO, M. WEINER, and G. SIMSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 775–779, Nov. 16, 1950. 10 fig., 15 refs.

Excessive degrees of hypoprothrombinaemia may be due either to an accumulation of dicoumarol in the plasma over a period of time or to an exaggerated sensitivity of the prothrombin-forming mechanism to low and short-lasting concentrations of the drug in the plasma. This paper records observations on the effects of water-soluble vitamin-K preparations on the two types. Four patients fell into the latter category in that they showed excessive prothrombin responses lasting for 5 days after the last dose, with only low or moderate dicoumarol plasma levels. In each of these a single intravenous dose of 75 or 112 mg. of water-soluble vitamin K caused the prothrombin time to fall to a safe level within 24 hours. (A figure shows this very prompt result.) Four other patients, with high plasma dicoumarol levels in 3 and moderate in 1, showed raised prothrombin times, high in 3 and moderate in 1. Water-soluble vitamin K was given intravenously in doses of 144 mg. in one case and about 72 mg. in the others. Repeated doses were required to reduce the prothrombin time to safe levels, as much as 720 mg. spread over 3 days being required in one case. It is suggested that the function of vitamin K in prothrombin synthesis may be interfered with through a competitive mechanism by dicoumarol. A high concentration of vitamin K would then overcome the competition, and where there was undue sensitivity of the prothrombin synthetic mechanism, a single dose might have effects sufficiently long-lasting to allow of the excess of dicoumarol being detoxicated. However, in cases in which the plasma dicoumarol level is high and may continue so for a considerable time, large doses of vitamin K will be required and must be repeated until the dicoumarol level has fallen. *Reginald St. A. Heathcote*

1802. **The Antiaccelerator Cardiac Action of Quinine and Quinidine**
O. KRAYER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 146–150, Oct., 1950. 3 figs., 5 refs.

In dog heart–lung preparations the cardiac acceleration produced by the infusion, at 3 μg. per minute, of L-adrenaline was inhibited by injecting quinine or quinidine. The inhibition was persistent and was not prevented by atropine. Irregularities of rate and rhythm were produced when a total of about 150 mg. quinine had been administered: at this stage the inhibition was about 80%, and 100% inhibition was not obtained. Doses approaching that which caused irregularities reduced the output of the preparation.

The antiaccelerator potency of quinine was about $\frac{1}{500}$ of that of veratramine, and its action less selective. *R. P. Stephenson*

1803. **Effect of Strophanthus on Coronary Blood Flow and Cardiac Oxygen Consumption of Normal and Failing Human Hearts**
R. J. BING, F. M. MARAIST, J. F. DAMMANN, A. DRAPER, R. HEIMBECKER, R. DALEY, R. GERARD, and P. P. CALAZEL. *Circulation* [*Circulation*] **2**, 513–516, Oct., 1950. 20 refs.

The effect of intra-arterial injection of strophanthus (0·65 mg.) or "strophosid" (0·5 mg.) on the coronary blood flow, cardiac output, and cardiac oxygen consumption was observed. The cardiac output was estimated from the results of heart catheterization, and the coronary blood flow by means of the nitrous oxide method. Observations were made on 7 normal subjects and 5 with cardiac failure. Strophanthus reduced cardiac output in the normal heart without affecting its oxygen consumption; in this way its efficiency was lowered. The oxygen consumption of the failing heart (per 100 g.) does not differ from normal. Strophanthus increased the cardiac output of the failing heart without affecting oxygen consumption, and therefore increased cardiac efficiency. No significant direct effect of strophanthus on the coronary vessels could be shown, since the coronary resistance remained unchanged after the administration of the drug. *H. E. Holling*

1804. **Multiple-balloon Kymograph Recording of the Action of Syntropan and of Trasentin on the Motility of the Upper Small Intestine in Man**
E. N. ROWLANDS, W. P. CHAPMAN, A. TAYLOR, and C. M. JONES. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **91**, 513–523, NOV., 1950. 5 figs., 13 refs.

The action of "syntropan" and "trasentin" on the activity of the small intestine was investigated by means of pressure recordings from the gut lumen. Four small balloons at intervals of 4 in. (10 cm.) were introduced into the duodenum and jejunum, from each of which pressure was recorded continuously by a water manometer. The duration of the experiments varied from 1 to 4 hours from the time of successful intubation. Altogether eight tests were made, during which one or other of the drugs was administered. On a further eight occasions the effect of placebos was investigated. Of the 4 subjects receiving syntropan, 2 received 30 mg. intramuscularly and 2 received 50 mg. by mouth. No significant difference in effect on tone or propulsive and non-propulsive intestinal activity was noted between those subjects receiving the drug and those receiving placebos. Similarly trasentin was given to 3 patients, who each received 150 mg. orally.

In addition one received 50 mg. intramuscularly. Here again there was found to be no significant difference between the effect of the drug and that of the placebos. Three of the patients receiving syntropan were also tested with belladonna alkaloids in standard doses. In every case a fall in tone and in propulsive and non-propulsive activity occurred within 40 minutes. The authors conclude that, as investigated by their method, syntropan and trasentin have no effect on small-intestinal activity. The belladonna alkaloids, however, have a marked and reliable antispasmodic effect.

A. G. Parks

1805. **The Histochemical Differentiation of Types of Cholinesterases and their Localizations in Tissues of the Cat**

G. B. KOELLE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 158–179, Oct., 1950. 23 figs., bibliography.

This paper describes the development of the author's technique (*Proc. Soc. exp. Biol., N.Y.*, 1949, **70**, 617) for the localization of cholinesterase (Ch.E.), which now enables specific and non-specific enzymes to be distinguished. In order to select suitable reagents for the differentiation, thio-analogues of various choline esters were tested as substrates for non-specific Ch.E. (horse serum) and specific Ch.E. (bovine erythrocyte) in the Warburg apparatus. Acetylthiocholine was hydrolysed more rapidly than acetylcholine by both enzymes: acetyl-β-methylthiocholine, unlike acetyl-β-methylcholine, was hydrolysed at a significant rate by non-specific Ch.E.; benzoylthiocholine, like benzoylcholine, was not split by specific Ch.E., and was split so slowly by the non-specific enzyme that it was unsuitable for the histochemical technique. Butyrylthiocholine, however, was split even more readily than acetylthiocholine by non-specific Ch.E. and was not attacked by specific Ch.E.

The inhibitors of Ch.E., " Nu 1250 " and " Nu 683 ", were found to be less selective against the two types of enzyme from cats than had been reported for other species; di-*iso*propylfluorophosphonate (DFP), however, completely blocked non-specific Ch.E. at a concentration of 10^{-6}M (benzoylcholine and butyrylthiocholine were no longer split by brain or serum Ch.E.), whereas the specific activity of brain (β-methylcholine hydrolysis) was only 40% inhibited. Some non-specific cholinesterase activity in liver survived concentrations of DFP which completely inhibited even specific Ch.E.

On the basis of these facts the histochemical technique previously described was modified. Tissue slices were incubated either with butyrylthiocholine, to show non-specific enzyme, or with acetylthiocholine after treatment with 10^{-6}M DFP, to show specific enzyme. The liberated thiocholine was precipitated as copper thiocholine at *p*H 6·4 as this was found to produce a sharper localization than was previously obtained at *p*H 8·0.

These techniques were applied to frozen sections of motor cortex and spinal cord; to sensory ganglia; to skeletal muscle; to the superior cervical ganglion, normal and denervated; to stellate nodose and ciliary ganglia; to terminal ganglia and effector organs in ileum, bladder, lung, adrenal gland, liver, and parotid gland; and to chemoreceptors in the carotid body. The results cannot be adequately summarized, but in general the central nervous system and skeletal muscle contained principally specific enzyme, while sensory ganglia, adrenal pericapsular ganglia, hepatic cells, and the carotid body contained principally non-specific enzyme. Some smooth muscle had predominantly one and some the other enzyme. Autonomic ganglia and effector cells contained both.

R. P. Stephenson

1806. **The Effect of Inhibition of Specific and Non-specific Cholinesterase on the Motility of the Isolated Ileum**

G. B. KOELLE, E. S. KOELLE, and J. S. FRIEDENWALD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 180–191, Oct., 1950. 6 figs., 36 refs.

The fact that di-*iso*propylfluorophosphonate (DFP) inhibits non-specific cholinesterase at lower concentrations than specific cholinesterase has been used to determine whether the non-specific enzyme plays a part in the activity of the ileum. Segments of ileum were removed immediately after death from cats killed by the intracardiac injection of air. The ileum was kept in Locke's solution at 8° C. for from ½ to 10 hours. The experiments were performed at 38° C. in a bath containing 200 ml. of Locke's solution with extra glucose. Freshly prepared dilutions of DFP were added in increasing concentrations. Finally, the muscle was removed and frozen and the remaining activity of specific and non-specific enzymes determined in the Warburg apparatus using acetylcholine, acetyl-β-methylcholine, and benzoylcholine as substrates. In addition, total and non-specific activities were localized in frozen sections by the authors' technique (see Abstract 1805).

Concentrations of DFP from 10^{-8}M to 10^{-6}M produced increased tone and sometimes increased the amplitude of spontaneous contractions. The cholinesterase determinations on the treated segments showed that this increased activity was accompanied by disappearance of non-specific cholinesterase activity; the specific activity was only appreciably reduced by 10^{-5}M DFP. The percentage activity remaining after treatment with DFP was as follows:

Molar Concentration of DFP	Total Enzyme %	Specific Enzyme %	Non-specific Enzyme %
10^{-8}	78	92	67
10^{-7}	66	98	31
10^{-6}	50	82	5
10^{-5}	31	40	6

Similar results were obtained when the tissue was first homogenized and then incubated with DFP.

The histochemical technique showed the longitudinal muscle to contain almost exclusively non-specific enzyme; this disappeared in segments treated with those concentrations of DFP which produced increased activity of the ileum.

R. P. Stephenson

1807. **Studies on Autonomic Blockade. III. Effect of High Spinal Anesthesia on the Vasodepressor Action of Veratrum in Human Subjects**
N. S. ASSALI and H. PRYSTOWSKY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 251–257, Nov., 1950. 3 figs., 15 refs.

Small doses of veratrine have previously been shown to cause a fall of blood pressure and cardiac slowing in patients with toxaemia of pregnancy as well as in normal subjects. These effects are equally well produced if procaine is given intrathecally in doses sufficient to cause cutaneous analgesia to the level of the 4th cervical segment and weakness of the limb and respiratory muscles. It is therefore unlikely that this action of veratrine is due to a stimulation of sympathetic vasodilator fibres. *V. J. Woolley*

1808. **Observations on Several *cyclo*Hexyl- and Phenylalkylamines**
E. J. FELLOWS, E. MACKO, and R. A. MCLEAN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 267–272, Nov., 1950. 7 refs.

The actions of 1-*cyclo*hexyl-2-aminopropane (A), -2-methylaminopropane (B), 1-phenyl-2-aminopropane (C), and -2-methylaminopropane (D) have been compared. A and B have less nerve-stimulating potency than C and D. In dogs under pentobarbitone, A and B have about half the effect of C and D in raising the carotid blood pressure. Determination of the volume of the nasal mucosa in dogs by an impedance method shows that D causes about the same degree of vasoconstriction as A when inhaled. It caused no irritation of the respiratory tract and daily injections of one-third of the LD 50 for 30 days caused no apparent damage to any organ. *V. J. Woolley*

1809. **Reversal of the Depressor Action of N-*iso*Propylarterenol (Isuprel) by Ergotamine and Ergotoxine**
A. M. LANDS, F. P. LUDUENA, J. I. GRANT, E. ANANENKO, and M. L. TAINTER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 284–297, Nov., 1950. 7 figs., 20 refs.

Small doses of ergotamine or ergotoxine enhance the pressor effect of adrenaline on " L-arterenol " and reverse the depressor effect of " isuprel ". Cardiometer readings and determinations of pulse amplitude show that the increased blood pressure is due to increased cardiac activity, accompanied by vasoconstriction. Similar but less marked effects are produced when the ergot alkaloids are combined with various other sympathomimetic amines which themselves have a weaker cardiac action. *V. J. Woolley*

1810. **The Pharmacological Activity of the Ring Methyl Substituted Phen*iso*propylamines**
D. F. MARSH and D. A. HERRING. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol*] **100**, 298–308, Nov., 1950. 2 figs., 34 refs.

Where given intravenously to dogs, whether unanaesthetized or under barbitone, 4-methyl-, 3-methyl-, and 2-methylphenyl*iso*propylamines have slightly less vasopressor potency than amphetamine; thus they have about $\frac{1}{200}$ of the potency of L-adrenaline. 3:4-Dimethyl- and 2:5-dimethyl-phenyl*iso*propylamine have $\frac{1}{3}$ to $\frac{1}{2}$ of their potency. All these compounds relax the isolated rabbit's intestine and guinea-pig trachea in a concentration of 1 : 4,000. The 2-methyl and 2:5-dimethyl compounds do not arouse mice under pentobarbitone; the other three derivatives have about half the effect of amphetamine. The 4-methyl derivatives have about half the effect of amphetamine. The 4-methyl derivative has the greatest effect in causing anorexia in man, this property being slight or absent in the others. *V. J. Woolley*

CHEMOTHERAPY

1811. **The Treatment of Various Infections with Terramycin**
E. R. CALDWELL, H. W. SPIES, C. K. WOLFE, M. H. LEPPER, and H. F. DOWLING. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 747–753, Nov., 1950. 1 ref.

This paper records the results of treatment with terramycin of 171 patients with various infections. In most of the adults terramycin hydrochloride was given in doses of 2·0 g. initially followed by 0·5 g. every 4 hours. Children were given 50 mg. per kg. body weight per day. The treatment was successful in 46 out of 48 patients with pneumococcal pneumonia (2 died), 14 with streptococcal infections, 7 with acute gonococcal urethritis, 7 out of 12 with urinary-tract infections, 3 with Vincent's infections, one case of herpes zoster out of a total of 59 cases of virus infections, and 22 out of a group of 28 miscellaneous cases. No serious toxic reactions were observed, although 25% of the patients had gastro-intestinal symptoms. One patient had transient vertigo. The drug had to be discontinued in 7 cases because of vomiting. *A. W. H. Foxell*

1812. **Effects of Terramycin on the Bacterial Flora of the Bowel in Man**
J. M. DI CAPRIO and L. A. RANTZ. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 649–657, Nov., 1950. 7 refs.

A dose of 750 mg. of terramycin hydrochloride or amphoteric terramycin was given orally to 7 patients every 6 hours for 2 to 22 days. The organisms found in the faeces before treatment started were coliform bacilli, non-haemolytic streptococci, and *Streptococcus faecalis*. Tests *in vitro* showed that most of the organisms were resistant to penicillin and sensitive to dihydrostreptomycin. All the organisms were sensitive to terramycin in a concentration of 5 μg. per ml. of medium, with the exception of *Proteus* and the yeasts. In all the patients the normal bacterial flora was either eliminated or greatly reduced in numbers within 48 hours of the start of treatment, and was supplanted by yeasts and *Staphylococcus pyogenes* var. *aureus*, coagulase negative. The normal flora returned a few days after withdrawal of the drug. Mild toxic disturbances of the gastro-intestinal tract

were seen in 5 of the 7 patients; in the urine of one of the patients a trace of protein and a few erythrocytes were found.

The authors conclude that the effectiveness of terramycin as an antimicrobial agent in the preparation of patients for surgical measures appears to be unexcelled.

A. W. H. Foxell

1813. **Interference of Aureomycin and of Terramycin with Action of Penicillin *in vitro***

J. B. GUNNISON, V. R. COLEMAN, and E. JAWETZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 549–552, Nov., 1950. 2 figs., 6 refs.

The action of penicillin, aureomycin, and terramycin, alone and in combination, on *Streptococcus pyogenes* and *Klebsiella pneumoniae* was examined by inoculating 1 ml. of an 18-hour broth culture of the test organism (10^7 to 10^8 cells) into 19 ml. of broth containing the antibiotics in various concentrations and proportions. During incubation at 37° C. 0·5-ml. quantities were removed at intervals and viable counts made.

The results showed that concentrations up to 10 to 50 μg. of aureomycin or terramycin per ml. interfered with the bactericidal action of penicillin on *S. pyogenes*. No interference could be shown if the first two substances were present in concentrations in which they were themselves bactericidal. The addition of a bacteriostatic concentration of aureomycin or terramycin to a bactericidal concentration of penicillin greatly decreased the death rate for *K. pneumoniae* during the first 7 to 12 hours. After 27 hours, however, the organisms exposed to such a mixture were no longer viable, whereas organisms exposed for a similar period to the same concentration of aureomycin or terramycin alone were likely to multiply. A similar interference with the action of penicillin *in vivo* has been demonstrated in preliminary experiments with mice.

It is suggested that since penicillin acts mainly on dividing cells, its bactericidal power may be impaired if cell division is inhibited by bacteriostatic concentrations of the other two antibiotics.

[This paper presents yet another argument against "blunderbuss" antibiotic therapy.]

J. E. M. Whitehead

1814. **The Relationship between Aureomycin, Chloramphenicol, and Terramycin**

F. E. PANSY, P. KHAN, J. F. PAGANO, and R. DONOVICK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 618–620, Nov., 1950. 14 refs.

A strain of *Bacterium coli* and a strain of *Staphylococcus pyogenes* were made resistant to chloramphenicol or aureomycin by subculture in increasing concentrations of the antibiotic. It was found that with the development of resistance to one, there was a small simultaneous increase in resistance to the other substance and also to terramycin. The mechanism of cross-resistance to antibiotics is discussed. *J. E. M. Whitehead*

1815. **Laboratory and Clinical Experience with Terramycin Hydrochloride**

W. D. LINSELL and A. P. FLETCHER. *British Medical Journal* [*Brit. med. J.*] **2**, 1190–1195, Nov. 25, 1950. 5 figs., 15 refs.

Terramycin is a pure amphoteric compound obtained from a soil actinomycete, *Streptomyces rimosus*. In contrast to aureomycin, it is relatively stable in solution, the sodium salt having an alkaline and the hydrochloride an acid reaction. Terramycin has a wide bacterial spectrum and is highly active *in vitro* against Gram-positive cocci and Gram-negative bacilli, inhibiting the growth of many of these organisms at concentrations of 0·25 to 0·5 μg. per ml. Most strains of *Pseudomonas aeruginosa* are relatively sensitive to concentrations as low as 5 to 15 μg. per ml., but *Proteus vulgaris* is highly resistant. The drug is administered orally in doses of about 50 to 70 mg. per kg. body weight daily. Therapeutic levels in the blood are usually maintained after such a dose for about 6 hours, and this is the recommended dosage interval for most purposes; it is, however, excreted in high concentration in the urine and adequate urinary levels can be maintained with a dose of 50 mg. daily. Therapeutic levels can be maintained in serous effusions, but penetration into the cerebrospinal fluid is very poor. On oral administration of 1 g. 6-hourly to 8 patients, striking changes were seen in the intestinal flora, the normal picture being replaced by a heavy growth of *Pr. vulgaris*, *Pr. morgani*, or a yeast. After the first 24 hours concentration of the drug in the faeces ranged from 500 to 4,000 (average 1,250) μg. per g.

In a small clinical trial the authors treated 13 cases of urinary infection, 4 cases of superficial skin infection, and 4 cases of post-operative infective complications, all of which responded well. A satisfactory response was also obtained in one of 2 cases of ulcerative colitis. Toxic symptoms occurring among the 33 patients who received the drug for 5 or more days included gastro-intestinal disturbances in 13 cases (severe in one only), an erythematous rash in one, and possibly a sore throat in one case. Terramycin was better tolerated when given with milk.

[This is the first report on terramycin that has been published in Great Britain and should be read in the original by all those interested in antibiotics. Terramycin should prove to be a useful addition to the drugs available for treatment of a wide variety of conditions, but supplies are certain to be very limited for some time to come.] *A. W. H. Foxell*

1816. **Aureomycin in the Treatment of the Common Cold**

R. J. HOAGLAND, E. N. DEITZ, P. W. MYERS, and H. C. COSAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 773–775, Nov. 16, 1950. 1 fig., 6 refs.

1817. **Effect of Aureomycin on the Stomach: a Gastroscopic Study**

C. S. LEWIS, T. C. BAUERLEIN, and H. M. SHYTLES. *Gastroenterology* [*Gastroenterology*] **16**, 586–588, Nov., 1950. 4 refs.

1818. **Therapeutic Assays of the Skin and Cancer Unit of the New York University Hospital. Assay IV. Aureomycin Hydrochloride Ointment**
H. H. SAWICKY, F. PASCHER, L. FRANK, and B. ROSENBERG. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 339–341, Oct., 1950. 5 refs.

1819. **Rhodomycin, a Red Antibiotic from Actinomyces** (Rhodomycin, ein rotes Antibioticum aus Actinomyceten)
H. BROCKMANN and K. BAUER. *Naturwissenschaften* [*Naturwissenschaften*] **37**, 492–493, Nov. 1, 1950. 1 fig.

From an unspecified strain of streptomyces a red antibiotic has been obtained, termed rhodomycin. The medium in which the organism is grown is extracted with acetone and the extract is then treated with hydrochloric or phosphoric acid: a red powder is obtained. Analysis gives its formula as $C_{22}H_{29}O_7N$: it is soluble in methanol and benzol, giving characteristic absorption bands. The solubility in water and picric acid is high, and a watery solution is inhibitory to the growth of *Staphylococcus aureus* in a dilution of 1 in 50,000,000. After oxidation with benzoquinone, naphthoquinone, and anthraquinone the product still possesses antibiotic activity.

G. M. Findlay

1820. **Antibacterial Substances in Seed Plants Active against Tubercle Bacilli**
R. Y. GOTTSHALL, J. C. JENNINGS, L. E. WELLER, C. T. REDEMANN, E. H. LUCAS, and H. M. SELL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 475–480, Nov., 1950. 11 refs.

In a previous paper (*J. clin. Invest.*, 1949, **28**, 920) the authors reported that among 161 species of seed plants, the extracts of 27 showed antibacterial activity against *Mycobacterium tuberculosis*. This paper describes some of the biological characteristics of two antibacterial extracts, the glycoside barbaloin from *Aloe vera* Linn. and a mixture of alkaloids from the roots of *Menispermum canadense* Linn. *Mycobacterium tuberculosis* and *Bacillus subtilis* were more sensitive *in vitro* to barbaloin than any of the other organisms tested: its activity was approximately halved if blood was added to the test medium. The alkaloid complex prepared from *M. canadense* showed most activity *in vitro* against *Myco. tuberculosis*, *Diplococcus pneumoniae*, *B. subtilis* and *Myco. phlei*, and this action was not inhibited by blood.

At present the toxicity of barbaloin and the alkaloid complex from *M. canadense* precludes their clinical application, but studies of a dimethiodide derivative of an alkaloid of this complex have shown that toxicity and antibacterial activity may be independent of each other.

Kenneth Marsh

1821. **The Antibiotic Action of Vitamin K.** (Sull'azione antibiotica della vitamina K)
V. TAVONI. *Ateneo Parmense* [*Ateneo parmense*] **21**, 56–71, Jan.–April, 1950. 16 refs.

Since Atkins and Ward in 1945 first observed the antibiotic activity of naphthoquinone derivates *in vitro*, an extensive literature on this subject has accumulated in Italy. In these experiments *in vitro* the bacteriostatic or bactericidal action of vitamin K (2-methyl-1 : 4-naphthoquinone) has been examined against *Brucella melitensis*, *Br. abortus*, *Pasteurella multocida*, *Staphylococcus aureus*, *Bacillus anthracis*, *Salmonella cholerae-suis*, *Streptococcus pyogenes*, and *Bacterium coli*. In a dilution of 1 in 500 vitamin K was bactericidal for all organisms; however, in dilutions of 1 in 1,000 and 1 in 2,000 a bactericidal effect could be demonstrated only with the first five micro-organisms; with the others only bacteriostasis was observed in 2 to 5 days. In dilutions of 1 in 3,000, 1 in 4,000, 1 in 5,000, and 1 in 10,000 bactericidal action was observed with the first 4 organisms, whereas bacteriostasis was demonstrable with the others up to a dilution of 1 in 5,000 within 1 to 6 days. In a dilution of 1 in 10,000 bacteriostasis was noticed only with *B. anthracis*. In dilutions of 1 in 20,000 and above no bactericidal effect was exhibited. Bacteriostasis occurred, however, within 1 to 20 days in a dilution of 1 in 20,000 in decreasing frequency in cultures of *Br. melitensis*, *Br. abortus*, *P. multocida*, *Staph. aureus*, and *B. anthracis*; in a dilution of 1 in 40,000 in cultures of *Br. melitensis*, *Br. abortus*, *P. multocida*, *Staph. aureus*; in a dilution of 1 in 50,000 in cultures of *Br. melitensis*, *Br. abortus*, *and P. multocida*; and in dilutions of 1 in 100,000 and 1 in 150,000 bacteriostasis was observed only in cultures of *Br. melitensis* and *Br. abortus*. In a dilution of 1 in 200,000 neither bactericidal nor bacteriostatic effect could be demonstrated.

Z. A. Leitner

1822. **Use of Antibiotics in the Treatment of Experimental Diphtheria Infections**
L. F. HEWITT. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 597–602, Oct., 1950. 4 refs.

Nine type strains of *Corynebacterium diphtheriae* were tested for their sensitivity to dihydrostreptomycin, to dihydrostreptomycin together with *para*aminosalicylic acid, and also to aureomycin and chloramphenicol. In tests *in vitro* serial dilutions of the antibiotics in papain digest broth, inoculated with 18- or 24-hour broth cultures of the strains, were assessed for their inhibiting capacity by the development of turbidity or surface pellicle. Dihydrostreptomycin inhibited growth in a concentration of 0·1 to 0·4 μg. per ml. Addition of *para*-aminosalycilate did not increase the inhibition. Under the same conditions 1 or 2 μg. per ml. of aureomycin and chloramphenicol were inhibitory. When 0·2 ml. of a broth suspension of a washed gravis strain was injected intradermally into guinea-pigs and the animal was treated at 2-hourly intervals with 4 subcutaneous injections, or at 6-hourly intervals with 2 doses orally, the first dose having been administered immediately before infection, only the animals treated with dihydrostreptomycin survived. Aureomycin, in this experiment, was capable of prolonging life. The single doses of aureomycin and chloramphenicol were 2 mg. and 5 mg. subcutaneously and 100 mg. orally, the single doses of dihydrostreptomycin being 5 mg.

In further experiments *in vitro* the *C. diphtheriae* strains were subcultured 40 times in broth containing sublethal doses of aureomycin or chloramphenicol without any appreciable development of resistance having been observed. Similar passages in dihydrostreptomycin

broth resulted in a 10,000-fold increase of resistance in 6 of 8 strains thus examined. Some strains also developed dihydrostreptomycin dependence which, however, seemed to be transitory. Toxigenicity remained uninfluenced by passage through broth containing antibiotics. Two gravis strains lost their capacity to ferment starch when passaged in dihydrostreptomycin broth.

In the discussion the author advocates the use of streptomycin or dihydrostreptomycin, and possibly aureomycin, for the clearance of diphtheria carriers. The fact that 2 gravis strains lost their capacity to ferment starch, together with the previously established fact that some gravis and mitis strains may belong to the same serological group and the great number of serological mitis groups, is regarded as supporting evidence for a hypothesis advanced earlier. This hypothesis postulated that the great number of serological mitis groups is due to mutation of gravis into mitis type strains.

K. S. Zinnemann

1823. **The Mode of Action of the Antibiotic, Usnic Acid**
R. B. JOHNSON, G. FELDOTT, and H. A. LARDY. *Archives of Biochemistry* [*Arch. Biochem.*] **28**, 317–323, Oct., 1950. 1 fig., 12 refs.

The antibiotic usnic acid was found to prevent the uptake of orthophosphate which is normally associated with the oxidation of various substrates by a washed residue of rat liver homogenate. In this respect its biological activity resembles that of certain other antibiotics and of dinitrophenol.—[Authors' summary.]

1824. **Experiments on the Neuro-toxic Effects of Streptomycin.** [In English]
E. CHRISTENSEN, H. HERTZ, N. RISKAER, and G. VRAA-JENSEN. *Acta Pharmacologica et Toxicologica* [*Acta pharmacol., Kbh.*] **6**, 201–218, 1950. 11 figs., 27 refs.

The authors, working at the University of Copenhagen, have investigated the action of streptomycin on the vestibular–auditory system, on which the antibiotic has an intrinsic toxic effect if daily doses are high enough and continued long enough. Guinea-pigs of 300 to 400 g. were used, and doses of streptomycin were administered subcutaneously once or twice daily for 4 to 6 weeks or until hearing was abolished or the animals died. Single injections of 100 mg. per kg. body weight daily for 23 to 28 days gave rise to no deaths and all 4 of the animals given this dose gained weight; among 9 receiving daily injections of 200 mg. per kg. there were 3 deaths, 7 out of the 9 lost weight (average 43 g.), and vestibular function disappeared between the 9th and 18th injections in 7 animals; among 17 receiving injections of 100 mg. per kg. twice daily there were 8 deaths, a progressive loss of weight in all cases, and loss of vestibular function in 10 animals after 10 to 15 injections; and among 12 receiving daily injections of 400 mg. per kg. there were 11 deaths and a considerable loss in weight (30 to 90 g.) in the 4 animals which survived after 1 week.

Histological examination of the central nervous system showed degeneration of vestibular and cochlear nuclei in the medulla oblongata parallel with the effects on hearing and vestibular function. In animals where both hearing and vestibular function were abolished, changes were also found in other nuclei of the medulla oblongata, in the Purkinje cells, in the cerebellum, and in the motor cells in the cortex. Severe poisoning also gave rise to changes in the vestibular ganglion, but none in the cochlear ganglion.

Malcolm Woodbine

1825. **Quantitative Estimation of the Toxic Effect of Streptomycin on Vestibular Function.** [In English]
H. HERTZ and N. RISKAER. *Acta Pharmacologica et Toxicologica* [*Acta pharmacol., Kbh.*] **6**, 219–226, 1950. 3 figs., 9 refs.

The main toxic effects of the antibiotics of the streptomycin group are paresis of the vestibular system, with vertigo, nystagmus, and loss of positional and vestibular reflexes. The authors have attempted to assess the vestibular reaction in guinea-pigs quantitatively, on the basis of the positional reflex of the head during, and immediately after, rotation, the movements of the head being recorded electrically. Recordings show the gradual irreversible loss of vestibular reaction in the case of streptomycin. With dihydrostreptomycin there is a partially reversible, diminished reaction (appearing at a late stage); there is normal deviation of the head at the end of the experiment, but with accompanying nystagmus.

Malcolm Woodbine

1826. **Fates of Some Antibiotics in the Rat. I. Penicillin and Streptomycin.** [In English]
K. PEDERSEN-BJERGAARD and M. TONNESEN. *Acta Pharmacologica et Toxicologica* [*Acta pharmacol., Kbh.*] **6**, 250–262, 1950. 5 refs.

The authors have investigated the fate of penicillins G and K and of dihydrostreptomycin when given by mouth and subcutaneously to normal rats and to rats which had been poisoned by the oral administration of 0·1 ml. each of carbon tetrachloride, ethanol, and water daily for 4 days in order to abolish the inactivating effect of the liver. To obtain the same concentration in the blood by oral administration, about 12½ times the subcutaneous dose of penicillin G had to be given to both normal and poisoned rats. The equivalent oral dose of penicillin K was about 7½ times the subcutaneous dose in normal rats and 5 times the subcutaneous dose in poisoned rats, equal doses giving a higher blood concentration in poisoned than in normal rats after oral administration. The equivalent oral dose of dihydrostreptomycin was 25 times the subcutaneous dose in both normal and poisoned rats. In liver-perfusion experiments in normal rats there was a considerable fall in penicillin concentration in the blood, that of penicillin K being reduced to 20% of the initial value after 90 minutes' perfusion and that of penicillin G to 60%; dihydrostreptomycin concentration, however, fell only to 84% of the initial value. In poisoned animals the results with penicillin G were the same, but with penicillin K and dihydrostreptomycin the effect of perfusion was much less. In ligated intestinal loops the concentration of penicillin G fell to about 22% of its original value within 15 minutes, and to 12% in 4 hours, while the reduction in concentration of dihydrostreptomycin was similar, but more protracted.

In the ligated rat's stomach there was a fall of 92·4% in penicillin-G concentration and of 27·6% in dihydrostreptomycin concentration in 4 hours. As penicillin G was not present in the blood at 2 or 4 hours, all of it must have been destroyed in the stomach. Dihydrostreptomycin, however, was present in the blood in concentrations of 10 μg. per ml. after 2 hours and 180 μg. per ml. after 4 hours. By comparison of the concentrations in the blood and gastro-intestinal tract at various intervals after oral administration it was determined that dihydrostreptomycin was less rapidly destroyed than penicillin, but much remained unabsorbed, 25% of the dose being excreted as such in the faeces in the 24 hours after its administration. *Malcolm Woodbine*

1827. **Quantitative Estimation of Benzaldehyde Thiosemicarbazone Derivatives ("TB I/698") in Serum, Exudates, and Urine on Oral and Parenteral Administration in Maximal and Therapeutic Doses.** (Quantitative Bestimmung von Benzaldehydthiosemicarbazonderivaten (TB I 698) in Serum, Exsudat und Harn bei oraler und parenteraler Belastung sowie bei therapeutischen Gaben)
—. INGEBORG and L. HEILMEYER. *Archiv für Experimentale Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **211**, 313–320, 1950. 9 figs.

The authors, having previously described a method for the estimation of "TB I/698" in body fluids, have now studied its concentration in serum and elimination in the urine in patients given the compound both orally and intravenously. The compound TB I/698 ("conteben" or thiacetazone) is acetylaminobenzaldehyde thiosemicarbazone. The single doses administered consisted of 100 mg. intravenously and 300 mg. orally, whereas repeated doses of 50 mg. were given two to four times daily by the oral route. On oral administration the maximum concentration in the serum occurred within 3 to 6 hours. [The example quoted gives a maximum concentration of 0·6 to 0·7 mg. per 100 ml.] The serum concentration was maintained for some time. After 24 hours there was 0·2 to 0·4 mg. per 100 ml. present, but after 72 hours only traces were found. About 30% of the dose was eliminated in the urine after 24 hours. The total amount excreted in 3 days was 40 to 50%. After intravenous administration a maximum concentration of 0·2 to 0·3 mg. per 100 ml. was obtained within 5 minutes and was then maintained for 2 to 4 hours, gradually falling to less than 0·1 mg. per 100 ml. after 36 hours. The elimination occurred in the urine to the extent of 60% in 2 days, and at the end of 3 days none of the compound was detectable in the urine. These studies are useful in helping to decide the amount and frequency of the doses to be given in the treatment of patients with tuberculosis. *R. Wien*

See also Sections Microbiology, Abstract 1909; Paediatrics, Abstract 1930; Cardiovascular Disorders, Abstract 1970; Genito-urinary Disorders, Abstract 2088; Infectious Diseases, Abstracts 2131–2; 2136–42; 2167(*a*), (*b*), and (*c*); 2175; 2177–8; and 2187; *Abstracts of World Surgery*, 1951, **9**, 237.

TOXICOLOGY

1828. **Toxicity of Sea Water in Mammals**
C. B. ALBRECHT. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 370–385, Nov. 1, 1950. 3 figs., 26 refs.

Sea water contains approximately 3·4% of sodium chloride, and its magnesium content is four times that which would cause death from cardiac arrest in mammals if present in serum, while those of Ca and K are about two-thirds of the fatal levels. The toxicity of various doses of sea water (actual or artificial solutions) and of solutions of urea, sucrose, magnesium chloride, and calcium chloride was investigated in rats, guinea-pigs, dogs, mice, and seals. The intraperitoneal route is the only one by which a large enough dose of sea water can be given to prove acutely fatal to small animals: an injection of 4 to 16% of body weight proved fatal to 75% of rats so treated. There was no difference between the mortality in groups of rats injected with sea water or with isosmotic salt solution, but with the latter treatment more animals had convulsions (possibly due to the depressant action of magnesium in sea water). If the dose of 15% of body weight of sea water or isotonic saline was concentrated twice by evaporation it proved more rapidly fatal when given by mouth or by injection. Rats injected with concentrated solutions of urea or sucrose also died, whereas if 16% of the body weight of sea water was diluted so as to be of normal tonicity and was injected intraperitoneally it did not prove to be lethal. Thus the osmotic pressure of the solution is of importance in determining its lethality. The magnesium ion contributes nothing to the toxicity of ingested sea water, but its depressant action contributes to the lethality of sea water given intraperitoneally. Measurements were made of the volume of intraperitoneal fluid and of body weight less urine and intraperitoneal fluid at various periods of time after injection of sea water, or of hypertonic saline, urea, or sucrose. It was concluded that the lethal effects of sea water given intraperitoneally are not due to circulatory failure, but to cellular dehydration with extracellular oedema, caused by excessive salt retention. The central nervous system is the tissue most sensitive to this change. Rats injected daily with sub-lethal doses of sea water or saline developed a degree of tolerance so that they survived subsequent administration of lethal doses. This tolerance developed in 3 to 4 days, but was equally quickly lost. It took the form of a diuretic reaction to treatment, which got rid of more chloride than in control animals. The amounts of sea water that rats would drink voluntarily were not deleterious to health. The only effective therapeutic measure was to dilute the injected sea water by giving injections of distilled water. Two dogs given 5% of body weight in sea water by mouth vomited after 20 minutes, but retained half of the chloride. Subsequent thirst was intense and water intake raised. Two seals were investigated and it was found that these animals do not normally swallow much sea water with their food, nor do they excrete higher urinary concentrations of chloride than are found in sea water. Their tolerance to sea water injected intravenously was no better than that of the rat, the mode of death being in depression, as in

magnesium anaesthesia. In man, sea water acts as an emetic, and if the subject is not dehydrated diarrhoea will follow. Coma or excitement may ensue. Petechial haemorrhages in gastric mucous membrane and in the peritoneal cavity of injected animals are due to the direct effect of hypertonicity. *James D. P. Graham*

1829. **Carbon Tetrachloride Mass Poisoning.** [In English]
A. ALHA. *Annales Medicinae Internae Fenniae* [*Ann. Med. intern. fenn.*] Suppl. 8, **39**, 1–32, 1950. 37 refs.

Details are given of the illness of 66 persons who consumed various quantities of a proprietary spirit hair-lotion which contained 1·4% of carbon tetrachloride in addition to the alcohol which attracted the patients in the first place. Immediate signs of toxicity took the form of gastro-intestinal irritation, vomiting of blood, diarrhoea, circulatory collapse, delirium, and disorientation leading to coma. Of the 20 patients who died, most showed haemorrhages and oedema, with parenchymatous degeneration of heart, liver, and kidneys. Death occurred within one week of taking the poison. Severe bronchitis was invariably present and several patients died of hypostatic pneumonia. Lower-nephron damage was severe enough to cause anuria and a number of deaths in uraemia. Liver damage was always present and varied from cloudy swelling to acute yellow atrophy. The power of regeneration of liver shown was remarkable. Symptomatic treatment only is possible.
James D. P. Graham

1830. **Appraisal of the Toxicity of the Gamma Isomer of Hexachloro*cyclo*hexane in Clinical Usage**
L. K. HALPERN, W. E. WOOLDRIDGE, and R. S. WEISS. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 648–650, Nov., 1950. 6 refs.

In view of reports implying that the gamma isomer of hexachloro*cyclo*hexane was not sufficiently safe for clinical use without further investigation, the toxicity of the gamma isomer was studied clinically. The toxicity in a control series was also investigated to ascertain its irritant and sensitizing capacities. The conclusion is not only that it is an excellent therapeutic agent with a very wide margin of safety, but that, on the basis of a small series of cases, the concentration of the gamma isomer may be reduced to well below 1% without sacrifice of clinical efficacy.
G. B. Mitchell-Heggs

1831. **Some New Facts concerning Chronic Carbon Monoxide Poisoning.** (L'oxycarbonisme chronique (données nouvelles))
A. BOURGUIGNON. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4449–4453, Nov. 22, 1950. 3 figs., 6 refs.

Investigations were made over a period of 4 years and 89 persons were examined. The symptomatology of chronic carbon monoxide poisoning is purely subjective. Asthenia, diminution of libido, giddiness, and headache are the most frequent complaints, and there may also be insomnia at night and sleepiness during the day, various digestive disturbances, loss of weight, and dyspnoea on effort.

In the series of cases described, carbon monoxide estimations in the blood, as made by Nicloux's method, generally gave figures of 5 to 10 ml. per l., but the carbon monoxide level did not always tally with the clinical picture. In view of this finding attempts were made to discover a more reliable index, and tests were made to determine the vestibular chronaxie by the author's method, testing one side only by means of an electrode in the auditory meatus and another over the mastoid process. On tilting the head various departures from normal readings were noted. Cochlear function, tested by the audiometer, showed a reduction for frequencies below 4,096. To exclude error by simulation the author's method of testing fatigue was used: in this a muscle is tetanized electrically, usually the biceps or vastus internus, and chronaxie is determined after the muscles have been tired in this way. The estimations made are shown diagramatically and suggest that this kind of investigation is of diagnostic value. When chronaxie studies were made on peripheral muscles, such as those in the hand, little change was observed except in the short abductors of the thumb, supplied by C8 to D1.

Treatment with "carbogen" gave but temporary relief and the blood carbon monoxide level rose again later, though work had not been resumed. Trans-cerebral and trans-medullary electrolysis with iodine was tried, but the general detoxicating action was not very marked. It was noted that cured cases quickly relapsed after fresh exposure to carbon monoxide if prophylactic measures were inadequate. Many chronic cases were apparently repeatedly poisoned by the use of tobacco. Many apparently well persons had blood carbon monoxide levels higher than those who were clearly suffering from poisoning, a puzzling phenomenon which the author does not try to explain. *G. C. Pether*

1832. **The Cause of Death from Excessive Pressure of Oxygen.** (Warum wirkt Sauerstoffüberdruck rasch todlich)
K. LENGGENHAGER. *Zeitschrift für die Gesamte Experimentelle Medizin* [*Z. ges. exp. Med.*] **116**, 353–377, 1950. 32 refs.

The theory that death during exposure to excessive oxygen pressures results from carbon dioxide retention in the tissues ("Haldane effect") and that the carbon dioxide-binding power of the blood is inversely proportional to its oxygen saturation is considered disproved for the following reasons: (*a*) Animals and men exposed to high oxygen pressures show none of the signs of carbon dioxide intoxication, such as "air hunger", The behaviour and mode of death of animals is fundamentally different in the two conditions. Subjective symptoms in man under high oxygen pressures differ from those in carbon dioxide poisoning. (*b*) In hyperventilation, when the blood is almost maximally saturated with oxygen, the symptoms are referable to carbon dioxide lack in the tissues rather than carbon dioxide accumulation (or hypoxia). (*c*) In men exposed to high

oxygen pressures the maximum time for which the breath can be held is actually increased. (*d*) It has been reported that in animals killed by high oxygen pressures the carbon dioxide content of artificial intraperitoneal air bubbles is considerably increased, but this is now proved to be a post-mortem phenomenon. (*e*) There was no significant increase in the carbon dioxide concentration in the spinal fluid of men exposed to high oxygen pressures long enough for symptoms to appear.

The theory that the effects of high oxygen pressures are due to inhibition of vital enzyme systems and/or the accumulation of toxic substances in the body could not be substantiated. Experiments with isolated organ preparations showed that high oxygen tensions have no deleterious effects on neuro-muscular transmission or the autonomous activity of the surviving frog's heart. The reinjection of blood and of brain-tissue extracts from animals dead with "oxygen poisoning" into other animals failed to demonstrate the presence of any toxic substances.

The absence of visible lesions in the tissues after death from oxygen poisoning is confirmed. Both the behaviour of animals and the subjective symptoms of humans exposed to high oxygen pressures suggest interference with cerebral function, which in view of (*b*) above is presumably a direct effect of the increased oxygen tension in the tissues. Thus animals show increased excitability, "clumsiness" in complicated movements such as jumping, and motor fits, while in men there occur fits of vertigo, disorders of vision, and hallucinations (but no mental confusion). The increased oxygen content of the cerebral tissues may interfere with intracellular reduction processes that are vital for the normal functioning of the cell. In support of this view it is shown that guinea-pig brain exposed to high oxygen pressures loses its power to reduce a coloured indicator such as indigo carmine (5 : 5′-indigodisulphonic acid).

[This is the weakest part of the paper as far as experimental proof is concerned. Thus, although isolated brain tissue loses its reducing power after exposure to high oxygen pressures, when the reduced form of the indicator is added to the brain of an animal dying of oxygen poisoning it remains in the reduced form, although it is itself a strong reducing agent. Similarly, if reduced indicator is injected during life and the animal is then killed by exposure to high oxygen pressures, the substance is found to be still in its reduced form after death. The experiment *in vitro* that seems to support the author's contention involved the exposure of the actual brain substance to an oxygen pressure (6 atmospheres) which is higher than any to which the brain would ever be exposed in the living animal.] *P. Mestitz*

1833. **Acute Poisoning with Potassium Bichromate**
C. N. PARTINGTON. *British Medical Journal* [*Brit. med. J.*] **2**, 1097–1098, Nov. 11, 1950. 3 refs.

The author reports 2 cases of potassium bichromate poisoning due to eating porridge made with contaminated oatmeal. Cyanosis, abdominal pain, vomiting, and diarrhoea were the only symptoms. The supernatant fluid of the cooked oatmeal was noticed to be yellow, and orange-red crystalline particles were seen on careful examination of the uncooked meal. Qualitative tests were positive, and a quantitative estimation showed the presence of 0·25% of the chemical contaminant. The source of the contamination could not definitely be established, but it is suggested that it may have been accidental, the parcel containing the oatmeal having been damaged during transmission by post and repacked. *Gilbert Forbes*

1834. **Successful Treatment of Cyanide Poisoning.** (Cyannatriumförgiftning och dess framgångsrika behandling)
H. HARTELIUS. *Nordisk Medicin* [*Nord. Med.*] **44**, 1747–1749, Nov. 3, 1950. 19 refs.

A case of acute cyanide poisoning is described. The patient had swallowed 4 grammes of sodium cyanide in order to commit suicide. His life was saved by the administration of oxygen and the intravenous injection of sodium thiosulphate.

The various forms of treatment mentioned in the literature are discussed. As adjuvants to oxygen, a combination of nitrites and sodium thiosulphate or of copper chloride and sodium thiosulphate is recommended by the writer.—[Author's summary.]

1835. **The Use of BAL in the Treatment of Skin Reactions due to Gold Therapy**
M. M. MONTGOMERY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 915–924, Oct., 1950. 19 refs.

1836. **Neuropathological Changes in Nitrogen Trichloride Intoxication of Dogs**
F. H. LEWEY. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 396–405, Oct., 1950. 6 figs., 13 refs.

THERAPEUTICS

1837. **The Efficacy of Oxygen Therapy, as shown by Measurement of Oxygen Consumption.** (Efficacité de l'oxygénothérapie determinée par la mesure de la consommation d'oxygène)
M. R. MALINOW, B. MOIA, and M. MANGUEL. *Acta Cardiologica* [*Acta cardiol., Brux.*] **5**, 457–472, 1950. 3 figs., 21 refs.

The effects of oxygen administration on the oxygen consumption, pulmonary ventilation, and pulmonary utilization of oxygen of 32 patients were examined. The patients were divided into four groups: (1) 10 patients without symptoms of cardiac insufficiency or coronary disease; (2) 14 patients with symptoms of coronary disease; (3) 14 with congestive heart failure (who included the 6 patients in group (4), the members of which group had both coronary disease and congestive failure). Five estimations were usually made on each patient; estimations lasted for 5 to 10 minutes and were separated by intervals of 5 to 10 minutes. The first estimation was generally rejected on account of the effects of emotion

and excitement. In the 2nd and 3rd atmospheric air was breathed, and in the 4th and 5th pure oxygen was inhaled.

No important changes in oxygen consumption could be attributed to the inhalation of oxygen. In certain cases a decrease occurred in pulmonary ventilation, indicated by an increase in oxygen utilization. Thus there is no objective evidence of any benefit to be derived from oxygen therapy by the patients studied.

F. A. Langley

1838. **Observations on Filatov's Tissue Therapy in 200 Cases.** (Notre expérience de la thérapie tissulaire de Filatov (d'après 200 observations))

L. Gosse and P. Martin. *Presse Médicale* [*Pr. méd.*] **58**, 1270–1271, Nov. 15, 1950. 3 refs.

Filatov's tissue therapy is based upon the hypothesis that living cells (animal, vegetable, or human) maintained in a state of survival under certain abnormal conditions produce " biogenic stimulants " which, if introduced into a living organism, excite certain vital reactions. The authors, working at the Nanterre Hospital, used subcutaneous implants of amnion and injections of placental extract, the preparation of which is described. Tissue implantation sites were chosen nearest to the disease process to be influenced. Occasional side-reactions were observed with the amnion, which was sometimes extruded as a foreign body or produced allergic manifestations. The 200 cases treated included examples of obliterative arteritis, painful amputation stumps, indolent ulcers and wounds, chronic polyarthritis, osteoarthritis, and delayed union of fractures. The authors claim relief of symptoms and improvement in a significant proportion of these cases, and suggest that the " biogenic stimulants " produce cellular auto-stimulation of a non-specific character.

I. Ansell

1839. **Aerosols II. The Role of Particle Size in Inhalation Therapy by Atomization and by Penicillin Dusts**

H. A. Abramson. *Diseases of the Chest* [*Dis. Chest.*] **18**, 435–449, Nov., 1950. 7 figs., 7 refs.

1840. **Adrenal Cortical Stimulation in Unspecific Protein Therapy.** [In English]

M. Schwartz. *Acta Allergologica* [*Acta allerg., Kbh.*] **3**, 227–245, 1950. 8 figs., 33 refs.

Investigations on patients undergoing fever therapy with intravenous injections of a vaccine, of milk, or of sulphur in olive oil, gave results which could only be attributed to increase in the production of adrenal cortical hormone. There was a short-lasting depression of circulating eosinophils, a moderate increase in urinary excretion of 17-ketosteroids, and an increase in the excretion of uric acid. It is suggested that the response in rheumatoid arthritis and allergic conditions to non-specific protein therapy is due to an increase in adrenal cortical function. It is also suggested that eosinophil counts should be used more frequently in fever therapy, both as a gauge of the degree of stress and as a test of pituitary–adrenal function.

A. W. Frankland

1841. **Intracardiac Blood Transfusion.** (О внутрисердечном переливании крови)

G. J. Prijma and I. L. Isaev. Вестник Хирургии имени Грекова [*Vestn. Khir. Grekov*] **70**, No. 3, 12–14, 1950. 1 fig.

Experiments on 21 dogs led the authors to believe that intracardiac blood transfusion is possible only into the left ventricle. Three anaesthetized dogs were maximally bled and one-half the amount of the blood obtained was mixed with potassium citrate and injected into the left ventricle. The animals survived and in the 2 weeks after the experiment showed no abnormality. Transfusion into the right ventricle always caused clotting and ventricular fibrillation. Puncture of the auricle or of the atrium caused bleeding into the pericardium and cardiac tamponade.

Z. W. Skomoroch

1842. **Kell–Cellano Blood Group System in Pregnancy and Transfusion**

J. B. Cochrane, R. H. Malone, and I. Dunsford. *British Medical Journal* [*Brit. med. J.*] **2**, 1203–1204, Nov. 25, 1950. 4 refs.

1843. **Temperatures Produced in Bone Marrow, Bone and Adjacent Tissues by Ultrasonic Diathermy. An Experimental Study**

P. A. Nelson. *Archives of Physical Medicine* [*Arch. phys. Med.*] **31**, 687–695, Nov., 1950. 6 figs., 11 refs.

Since the observations of Freundlich *et al.* in 1932 on the heating effects of ultrasonic radiation on the marrow of a chicken bone, very little work has been reported on this subject. In an endeavour to assess the relative heating produced by ultrasonic waves in living tissues and possible application of this form of heating to medicine, the author has conducted a series of experiments on dogs. He used ultrasonic radiation at an output of 5 and 10 watts on anaesthetized dogs and compared the heating effects in muscle, bone cortex, and bone marrow with that produced by microwave diathermy. With microwaves the highest temperatures were observed in muscles, whereas with ultrasonic radiation significantly higher temperatures were observed in bone cortex and bone marrow after an application of only 1·5 minutes. No observable gross damage to superficial tissues was noted. The increase in temperature averaged 1·1° C. in muscle, 5·9° C. in bone cortex, and 5·4° C. in bone marrow. During the majority of the experiments no serious difficulty was encountered in obtaining constant readings with a variance of not more than 1 to 2° C. However, on a few occasions widely divergent readings were obtained for no apparent reason, and the author emphasizes the point that a rather wide margin of safety with regard to dosage is necessary on account of these unexpected variations that not infrequently arise. If ultrasonic radiation proves in the future to be a useful form of medical diathermy it would seem most likely that its use would be limited to the treatment of small circumscribed lesions such as those of certain forms of chronic osteomyelitis which have proved resistant to antibiotics.

M. H. L. Desmarais

Radiology

1844. **Sulfhydryl-containing Agents and the Effects of Ionizing Radiations. I. Beneficial Effect of Glutathione Injection on *X*-ray Induced Mortality Rate and Weight Loss in Mice**

W. H. CHAPMAN, C. R. SIPE, D. C. ELTZHOLTZ, E. P. CRONKITE, and F. W. CHAMBERS. *Radiology* [*Radiology*] **55**, 865–873, Dec., 1950. 2 figs., 35 refs.

Experiments were carried out on 50- to 60-day-old Swiss albino mice weighing 20 to 25 g. divided into 6 groups, each containing equal numbers of males and females. Group (A) received total body irradiation only; group (B) were given two injections of glutathione, the first 24 hours, and the second immediately, before irradiation (a total of 15 mg. glutathione); group (C) received a single injection immediately before, and a single injection immediately after, irradiation (a total of 40 mg. glutathione); group (D) received injections of isotinic saline (in amounts equal to the volume of glutathione injection) and total body irradiation; group (E) received injections of glutathione alone; and group (F) were untreated. All irradiated mice received a total body dose of *x* rays of 800 r.

The survival rates of glutathione-injected mice (63·8%) were greater than those in the comparable control groups (40 to 46%), the differences being statistically significant. Furthermore, the glutathione-treated irradiated mice lost less weight, and recovered weight more rapidly, than the surviving irradiated controls, and the mortality among these glutathione-treated survivors, when traumatized, was lower than in non-treated controls.

J. J. Mathews

1845. **Further Studies of the Beneficial Effect of Glutathione on *X*-irradiated Mice**

W. H. CHAPMAN and E. P. CRONKITE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 318–322, Nov., 1950. 8 refs.

Glutathione and cysteine afford some protection to animals against whole-body *x*-irradiation, and the protective action of cysteine is related both to the dosage of the amino-acid and to that of the *x* rays. In this communication the authors report a series of experiments in which mice, some treated with glutathione and others untreated, were irradiated and the dosage-mortality, weight change, and effect of controlled trauma on surviving irradiated animals in the two groups compared. Radiation was provided by a 2,000-kVp. *x*-ray beam (1·5 ma., no added filter, 15 r per minute in air at 2 metres; H.V.L. 4·3 mm. Pb), and doses of from 550 r to 1,150 r (air) whole-body irradiation were given to various groups of male inbred Swiss albino mice weighing 20 to 25 g., 2,343 mice being used in all. Glutathione (GSH) was injected subcutaneously as a 10% aqueous solution at *p*H 6·5 into two of the groups, one receiving 1·6 mg. per g. body weight, the other 4·0 mg. per g.; controls received saline at the same *p*H, and injections were given 5 to 30 minutes before irradiation. For each of the above groups there was a comparable non-irradiated or non-injected control group. Mortality rates and weight changes over a 28-day observation period were recorded in each experiment, and on the 29th day survivors were subjected to controlled trauma in a Noble–Collip drum.

For the untreated irradiated mice the 28-day LD 50 was 740 r; for those receiving 1·6 mg. glutathione per g. it was 840 r; and for those receiving 4 mg. glutathione per g., 950 r. The proportions surviving 950 r were: 2·9% of 68 untreated mice, 12·5% of 48 mice given 1·6 mg. glutathione per g., and 65·6% of 30 mice given 4 mg. per g. In the glutathione-injected groups the animals lost less weight, and the mortality from controlled trauma among the survivors was less, than in the untreated controls. In mice irradiated with less than 650 r no significant difference in mortality was found between the groups.

The authors conclude that the smaller weight loss, the lower susceptibility to trauma, and the higher survival rates among mice given glutathione indicate either that less injury is sustained per unit of radiation by these animals or that their recovery from the effects of radiation is accelerated.

Arthur Jones

1846. ***In vivo* Localization of Radioactive Silver at Predetermined Sites in Tissues. Preliminary Report**

H. D. WEST, R. R. ELLIOTT, A. P. JOHNSON, and C. W. JOHNSON. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 831–834, Nov., 1950. 14 refs.

The authors describe, in this preliminary report, the technique employed in a study of the localization of long-half-life radioactive silver after injection into albino rats. By first infecting the animal by injection of a culture of *Staphylococcus aureus* and injecting the radioactive silver 48 hours later they were able to show that the silver concentrates at the site of induced infection in significant amounts. A possible explanation for this concentration is that the silver, being transported by the leucocytes, concentrates in the areas where there is active phagocytosis.

H. C. Warrington

1847. **An Experimental Study of the Cardiovascular Effects of Diodrast**

A. J. GORDON, S. A. BRAHMS, S. MEGIBOW, and M. L. SUSSMAN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 819–830, Nov., 1950. 2 figs., 12 refs.

Dogs anaesthetized with pentobarbitone and given forced intravenous injections of 20 ml. of a 70% solution of diodone invariably developed a typical reaction, consisting of a rise, followed by a fall, in arterial blood pressure, a rise in pulse pressure associated with marked changes in the contour of the femoral arterial pulse

tracing, a rise in venous pressure, a fall in the pulse rate, and changes in the electrocardiogram. Similar results, but not so pronounced, were obtained with a 35% solution of diodone. This typical reaction could be modified, but never completely suppressed, by reducing the speed of injection. The most significant of these effects were probably due to vasodilatation, while stimulation of the cardiac muscle, followed by depression, also appeared to occur. Two dogs developed pulsus alternans.

Efforts to prevent the vasodepression failed. These included abdominal compression, the administration of sympathomimetic drugs (adrenaline, ephedrine, etc.) and vasopressin, parasympathetic block by means of atropine and vagotomy, and the administration of tetraethylammonium chloride and of an antihistaminic. There was no evidence of allergic sensitization in dogs which received two injections at an interval of several weeks.

A. Orley

RADIOTHERAPY

1848. **A Practical Method of Rotational Radiotherapy.** (Radiothérapie rotatoire)

A. HERVÉ. *Journal de Radiologie, d'Electrologie, etc.* [*J. Radiol. Electrol.*] **31**, 551–556, 1950. 8 figs., 21 refs.

The theoretical advantages of rotational therapy are briefly outlined and the importance of Nielsen's "coefficient of efficiency", which is the ratio of axial to surface dose, is stressed. An experimental investigation of the factors affecting this ratio was made in which a cylindrical wax phantom 26 cm. in diameter and 15 cm. high was used. This was rotated in an *x*-ray beam and measurements were made at various levels by means of a "victoreen" ionization chamber. The chief findings were as follows: (1) Size of field. Contrary to experience in conventional therapy the above ratio was increased with small fields. (2) Diameter of phantom. For any given radiation there was a certain diameter for which the ratio was a maximum. (3) Quality of radiation. The optimum ratio was obtained with a radiation of H.V.L. 1·7 mm. Cu. With harder radiation the ratio was diminished owing to a higher emergent dose at the distal surface of the phantom. (4) A focal distance of 40 to 50 cm. was found to be the optimum.

The spatial distribution of dose within the phantom is shown for asymmetrical arrangements where the axis of the beam does not pass through the centre of the phantom; the importance of correct alignment is emphasized. An apparatus for rotational therapy is described. The lesion is visualized radiographically on a fluorescent screen which is viewed by a minor during treatment, the irradiation risks being thus minimized. The treatment chair can be moved in both horizontal axes by a system of electric motors, and correct alignment thus maintained throughout the treatment. No attempt is made to give an analysis of clinical results. The advantages claimed are accurate alignment even with small fields, and constant maintenance of the lesion in the *x*-ray beam.

D. G. Bratherton

1849. **Some Observations with 1,000-kV. and 200-kV. *X*-ray Therapy**

W. T. MURPHY and M. C. REINHARD. *Radiology* [*Radiology*] **55**, 477–493, Oct., 1950. 15 figs., 2 refs.

The authors describe observations made during the treatment of cases of carcinoma of the cervix with *x* rays at 200, 400, and 1,000 kV and compare various aspects of their results. The half-value layers of the tubes used were 0·9, 5·0, and 9·0 mm. Cu. respectively. Skin effects were very similar for all three voltages, but in cases treated with the 200-kV tube the late effects on the skin were probably more pronounced than when the 1,000-kV tube was used. If the dose per exposure was increased and each field only treated every 4 days, thus keeping the total dose and over-all treatment time constant, then skin changes were more marked for all three qualities of radiation but the difference seemed to be greater in cases receiving 200-kV radiation. The depth dose received was greater and where gamma irradiation was used to supplement the *x*-irradiation a greater incidence of bladder and rectal reactions was experienced in cases treated with the 1,000-kV tube than in the others. Three-year results for the three groups were as follows: 200 kV (891 cases), 43·1%; 400 kV (79 cases), 45·5%; 1,000 kV (168 cases), 48·8%. In view of the wide quantitative and qualitative differences between the above three groups, the authors compared results in an equal number of cases of stages II and III selected from the 200-kV and 1,000-kV groups. The 3-year survival rates for these were 45·6% and 58·5% respectively.

J. M. W. Gibson

1850. **Recurrence of Carcinoma of the Cervix after Combined Radium and *X*-ray Treatment.** (Über die rezidive des Kollumkarzinoms nach kombinierter Radium-Röntgen-Bestrahlung)

J. RIES and J. BREITNER. *Zeitschrift für Geburtshilfe und Gynäkologie* [*Z. Geburtsh. Gynäk.*] **133**, 297–331, 1950. 5 figs., bibliography.

This paper records the results of an inquiry into the causes of failure in the treatment of carcinoma of the cervix by combined radium and *x*-ray therapy. In 524 cases, constituting 45% of a total of 1,165 patients treated at the Gynaecological Clinic of Munich University during the years 1938–41, the condition responded to treatment but recurred, while in a further 105 patients it failed to respond even temporarily. In the overwhelming majority of the latter group the disease was in stage III or IV; this is taken by the authors to indicate that there are hardly any primarily radio-resistant cervical carcinomata and that it is the extension of the growth and its relation to the body as a whole, rather than its histological structure, which determine the success or failure of radiation treatment.

The 524 recurrent cases were distributed over the four clinical stages as follows: stage I: 97 cases (37% of all stage-I cases). Stage II: 149 cases (44·5%). Stage III: 250 cases (51%). Stage IV: 28 cases (37·2%). From an analysis of the whole series according to the patient's general condition it was apparent that cancer of the

cervix not infrequently attacks patients in excellent general condition, and also that the results of treatment in this series were best in those patients classed as "obese". This is remarkable in view of the reduced *x*-ray dose received at the tumour in stout patients and it is suggested that the co-existent endocrine hypofunction present in the great majority of such cases may have a beneficial influence on the ultimate treatment results. It is also shown that in each stage the prospects of a permanent cure run parallel with the general state of health, and that the prognosis in cachectic patients is extremely grave, irrespective of the clinical stage of the disease.

Over 40% of all recurrences developed within the first 6 months after treatment, after which life expectancy increased markedly with each successive year, only 5% of those patients who survived 4 years subsequently developing a recurrence. The parametrium was the site most frequently affected by a recurrence, a preference for the right side being explained as being due to development asymmetry, as a result of which the left parametrium remains always shorter than the right; the radiation dose received by the left parametrium from radium situated, in most cases, to the left of the mid-line is therefore considerably higher than on the right, and the development of a recurrence on that side less likely. The supraclavicular ("Virchow's") lymph nodes were found to be involved in 4 out of the 26 cases with extrapelvic metastases, and should always be looked for. Re-treatment of pelvic recurrences is advised as, in spite of the very poor ultimate results (1·9% 5-year survival), it produces subjective improvement and some prolongation of useful life. *Jan G. de Winter*

1851. **Treatment of Infiltrating Carcinoma of Bladder by "Retrograde Method of Interstitial Radiation"**
T. B. WAYMAN. *Journal of Urology* [*J. Urol.*] **64**, 469–483, Sept., 1950. 11 figs., 3 refs.

The author describes his technique of interstitial irradiation in the treatment of infiltrating carcinoma of the bladder, in which the radium or radon is inserted without opening the bladder. Three methods of approach have been used: for many tumours a suprapubic approach is satisfactory, but a vaginal approach has also been used in tumours situated near the trigone in females, and a perineal approach for similar tumours in males. "Vaseline" gauze is used in each case to protect neighbouring structures from irradiation. The 7 cases in which the technique has been used are reported. Satisfactory results are claimed in 4 of these, in which the period of observation ranged from 2 to 21 months, but the author emphasizes that the efficacy of this method cannot be determined until a large series of cases have been treated. *Victor W. Dix*

1852. **Failure of Prophylactic Irradiation after Surgical Removal of a Keloid.** (Fracaso de la irradiatión preventiva después de la extirpación quirúrgica de un queloides)
X. VILANOVA, J. OLLER COROMINAS, and F. FORNES. *Actas Dermo-Sifiliográficas* [*Actas dermo-sifiliogr., Madr.*] **42**, 35–38, Oct., 1950. 1 fig.

RADIODIAGNOSIS

1853. **Tumors of the Esophagus below the Mucosa and their Roentgenological Differential Diagnosis**
R. SCHATZKI and L. E. HAWES. *Review of Gastroenterology* [*Rev. Gastroent.*] **17**, 991–1014, Nov., 1950. 19 figs., 15 refs.

In a previous article (*Amer. J. Roentgenol.*, 1942, **48**, 1) the authors described the appearance of 6 extramucosal oesophageal tumours, 3 of which were verified at operation. The present paper summarizes these 6 cases and adds 5 further ones, all of which were verified anatomically. The 8 verified cases consisted of 2 neurofibromata, 2 leiomyomata, 3 cysts, and 1 haematoma following the injection of oesophageal varices.

The main difficulty in diagnosis is to decide whether a lesion lies in or outside the oesophageal wall. Most filling defects from outside pressure are easily recognized as due to a tortuous aorta or to a bronchus. Inflamed lymph nodes in the tracheal bifurcation sometimes create an insoluble problem, but temporizing prevents unnecessary operation. Mucosal tumours are unlikely to be mistaken for extramucosal ones. Extramucosal lesions usually interfere little with the elasticity of the oesophagus and they produce a soft-tissue mass which indents the lung transparency. Mucosal lesions are usually extensive, as well as ulcerated and irregular. A malignant extramucosal tumour ulcerating into the oesophagus would probably be indistinguishable from a carcinoma. A very early and small carcinomatous plaque presumably might be mistaken for an extramucosal tumour, but in practice early oesophageal carcinomata cause no symptoms.

(In the discussion there was agreement that whereas in cases of carcinomata the presenting symptom is usually difficulty in swallowing, pain occurring only later, in cases of extramucosal tumours the presenting symptom is substernal discomfort or pain.)
Denys Jennings

1854. **Cardiological Case-finding by Means of Mass Miniature Radiography**
P. O. LEGGAT. *British Medical Journal* [*Brit. med. J.*] **2**, 1364–1366, Dec. 16, 1950. 2 figs., 3 refs.

The material for this report was obtained from two surveys, the first group of 11,929 subjects, being mainly industrial workers in factories, and the second, of 244 women, being patients in a mental hospital.

For the diagnosis of cardiac abnormalities from the miniature *x*-ray film the following criteria were adopted; enlargement of the cardiac shadow; undue prominence of the pulmonary artery; changes in the contour of the aortic arch and cardiac shadow; congestive changes in the lung fields. A considerable number [unspecified] of persons with such signs who were recalled for large-film and clinical examination were found to be perfectly normal.

In the first survey 22 cases of rheumatic heart disease were identified through the use of mass miniature radiography, 17 of which had already been diagnosed by other means before the survey. There were 14 instances

of hypertensive heart disease, none of which had been diagnosed before the mass radiological survey, and there were, in addition, 8 cases of congenital heart disease, 7 of which had been previously diagnosed. In the second survey, in the mental hospital, only 2 cases of rheumatic heart disease were diagnosed radiologically, although from the clinical examination on admission to the hospital there were known to be 11 cases. In this group there were also 4 cases of hypertensive heart disease, of which only one was diagnosed by means of mass miniature radiography.

It is concluded, therefore, that mass miniature radiography is of some, though limited, value in the diagnosis of cardiac abnormalities, and that by its means some cases of cardiac disease with few or no symptoms may be revealed. It is obvious that in such surveys a large number of cardiac cases must be missed. *L. G. Blair*

1855. **Radiological Features of Aneurysm of the Heart.** (Röntgenologische Betrachtungen bei Aneurysmabildung des Herzmuskels)
W. HIRSCH. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **73**, 525–536, Oct., 1950. 9 figs., 18 refs.

The characteristic radiological appearance in cases of cardiac aneurysm is that of a bulge of the cardiac wall, the size of which varies according to the extent of the area of myocardial necrosis or fibrosis, usually due to coronary occlusion, of which the aneurysm is the result. Cardiac aneurysms may be acute or chronic. The acute condition may be due to a sudden increase of pressure causing tearing of the myocardium or even rupture of the cardiac wall. Myocardium has no regenerative power and, if the patient survives, a connective-tissue scar forms, in which a chronic aneurysm may develop. Aneurysms develop most commonly on the left anterior surface of the heart near the apex, much less commonly on the posterior wall of the left ventricle, and seldom on the wall of the right ventricle or on the walls of the auricles. Males are affected twice as commonly as females.

Diagnosis is seldom possible *in vivo*. Investigation should include radiography and electrocardiography, in addition to the history of the patient and clinical findings, while the diagnosis may become clear from the course of the disease. In radiological examination both fluoroscopy and radiography should be employed, while kymography may be of value. On screen examination the site and shape of the lesion must be observed together with the function of the affected site and the behaviour of the neighbouring organs. A small bulge of the anterior left ventricular wall near the apex, the size of which may reach even the size of a hen's egg, is typical. The heart is not necessarily enlarged to the left. Very often the bulge is seen as a second contour of the left border of the heart, while sometimes the aneurysm may show as an enormous enlargement of the left heart without the right heart being affected at all, but these appearances are not the rule. *X*-ray examination may be completely negative for some time, the appearances subsequently becoming characteristic. The author describes the characteristic fluoroscopic appearances on performing Valsalva's or Muller's tests, but since the sudden increase of blood pressure may cause the rupture of the aneurysm it is inadvisable to carry out these tests. On the screen the aneurysm shows a very superficial pulsation or no pulsation at all, kymography confirming this finding and showing that pulsation is much decreased in the area of infarction. The author quotes Steel who maintains that the pulsation of the aneurysm is not due to contraction of the cardiac muscle in the part affected, but to bulging of the weakened area during systole. Calcification of the aneurysmal wall may take place in chronic cases, the calcified aneurysm behaving like a foreign body in the cardiac wall.

Radiographs in cases of cardiac aneurysm must be taken with good penetration by the spot-film device or with the Bucky diaphragm. In such films calcification of the wall is well shown. Lesions to be considered in the differential diagnosis are: (1) aneurysm of the ascending or descending aorta; (2) aneurysm of the pulmonary artery; (3) tumours and cysts of the epicardium, myocardium, or pericardium; (4) diverticula and herniation of the pericardium; (5) tumours and cysts of the mediastinum; and (6) encysted pleural effusion. In the presence of calcification constrictive pericarditis (*Panzerherz*) must also be taken into consideration. *W. J. Czyzewski*

1856. **Roentgenologic Aspects of Diffuse Miliary Granulomatous Pneumonitis of Unknown Etiology. Report of Twelve Cases with Eighteen Months' Follow-up**
B. FELSON, G. F. JONES, and R. P. ULRICH. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 740–746, Nov., 1950. 3 figs., 20 refs.

The roentgenological findings observed in an unusual epidemic of an acute illness encountered in 12 men who had been engaged in cleaning an abandoned water tower are presented. Widespread miliary lesions were demonstrable in the lungs of all 12 patients. Although clinical recovery was rapid, the roentgen changes regressed slowly. In 4 of the 12 cases minimal pulmonary involvement was still detectable from 14 to 18 months after onset. The cause of the epidemic was not established. Reports of three similar epidemics were encountered in a review of the literature.—[Authors' summary.]

1857. **Tomographic Study of the Bronchi Draining Tuberculous Cavities.** (Studio stratigrafico dei bronchi di drenaggio delle cavità tubercolari)
C. FRANCHINI and A. MORGANA. *Radiologia Medica* [*Radiol. med., Torino*] **36**, 818–828, Oct., 1950. 11 figs., 22 refs.

This paper is based on a series of over 3,500 tomographic examinations of tuberculous lesions of the lungs performed at the Sondalo Sanatorium Village and the Institute of Radiology of the University of Pavia. In most cases a standard technique was used, but in some the patient was tilted into a position such that the bronchus draining the affected area was parallel to the

table in order to demonstrate its entire length; in some cases a lateral projection was also used. Usually the bronchus draining an apical cavity leaves it at its inferior margin, whereas those draining the less common middle-third and basal cavities leave at the medial and superior margins respectively. Sometimes two or more bronchi drain a large cavity and then unite; but if the large size of the cavity is due to tension from valvular stenosis there will be a single draining bronchus. In well-drained cavities the junction with the bronchus is abrupt, giving a typical " tennis-racket " shape; in others it is ill-defined, producing a funnel shape, probably due to necrosis around stagnant material.

The authors divide the specific bronchial lesions into three main types: (1) exudative or caseous; (2) productive or granulomatous; and (3) ulcerative. They give some details of the pathology of each type. Radiologically, the exudative type shows accentuation of the parallel-line shadows. When the condition progresses to caseation there will be irregular thickening of the walls and possibly obliteration of the lumen. The ulcerative type shows dilatation of the bronchi with thinning of the walls and perhaps small cavities due to herniation between the cartilages. Association of bronchial with peribronchial lesions, particularly of the caseous or granulomatous types, causes the disappearance of the bronchial lumen with formation of uniform, ribbon-like shadows.

The tomographic examination of the draining bronchus may provide answers to some interesting questions, such as the following: (1) When the sputum becomes negative after collapse therapy, is this due to closure of the cavity or to angulation and stenosis of the bronchus? Probably both factors are usually involved, but stenosis of the bronchus precedes closure of the cavity. (2) Formation of tension cavities. These may follow collapse therapy or be due to extrinsic and intrinsic organic factors affecting the bronchus, such as partial block by caseous material. The draining bronchus becomes obscured by an atelectatic zone and the cavity is ball-like, with a smooth, well-defined wall. (3) Spontaneous closure of cavities. Moreover, recognition of a draining bronchus helps in differentiation between cavities and pseudo-cavities such as emphysematous bullae and in the detection of cavities in the course of collapse therapy. Study of the draining bronchus may also influence treatment; for example, unsuccessful collapse therapy may occlude a partially stenosed bronchus and produce a tension cavity: in such cases the use of Monaldi's drainage should be considered or attention directed towards improving the bronchial condition before intervening with collapse therapy with undesirable results. *Sidney J. Hinds*

1858. **The Bronchogram in Pulmonary Emphysema.** (Il broncogramma nell'enfisema polmonare)
S. SCARINCI. *Archivio di Tisiologia* [*Arch. Tisiol.*] **5**, 659–669, Aug., 1950. 11 figs., 9 refs.

The author points out the frequency with which patients with chronic dyspnoea diagnosed clinically as due to emphysema are found at necropsy to have normal alveoli. He emphasizes the importance of the bronchogram in arriving at an exact diagnosis and describes his technique of investigation of cases of dyspnoea of the emphysematous type, with reference to 4 illustrative cases. Films are taken at 5, 20, and 45 minutes, and again at 6 hours, after the injection of the contrast medium. This is done in order to avoid interpreting filling limited to the bronchi as pathological when it was in fact a normal appearance. The first film in both normal and emphysematous subjects shows filling of the bronchi only, and is described as having the appearance of a dead tree. Subsequent films in normal subjects show alveolar filling which the author describes as resembling a tree in summer complete with all its foliage, whereas in emphysema they show filling of the larger bronchi only, the bronchioles and alveoli remaining empty as in the first film. The author claims that the " lily of the valley " appearance previously described as being due to incomplete filling of normal alveoli is in fact due to a lobular emphysema. *John H. L. Conway-Hughes*

1859. **Roentgenological Diagnosis: Generalized Subserous Emphysema through a Single Puncture**
M. RUIZ RIVAS. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 723–734, Nov., 1950. 26 figs.

The author describes and illustrates the pelvic, abdominal, thoracic, and cervical subserous cellular tissues, their points of inter-communication and communication with the deep tissues of the limbs, and the technique of their radiological demonstration by means of a single injection of gas, in this case, oxygen. The point of injection is at the level of the sacrococcygeal joint, 1 or 2 cm. beyond the inferior border of the sacrum. The needle is directed obliquely upwards, inwards, and forwards in such a way that its point comes to rest in the presacral cellular tissue or the retrorectal space as near as possible to the anterior surface of the sacrum and in the midline. It is advisable to ascertain that the point of the needle is in the pararectal tissue and has not penetrated a blood vessel. A small quantity of air is then injected and if this can be carried out with ease the insufflation will be successful. If resistance is encountered the position of the point of the needle should be altered. The patient may be in any position, but the author prefers the genupectoral. From the pelvic cellular tissues the gas gradually advances into the abdominal cellular tissue, outlining the kidneys, adrenals, liver, and spleen, and occasionally also the small and large intestines. The diaphragm and its muscular insertions are clearly outlined. The demonstration by emphysema of the mediastinum is of no great diagnostic value; on the other hand, the various organs of the neck are clearly outlined. Any inconvenience caused by the emphysema disappears within a few hours. *A. Orley*

1860. **Radiological Appearances in Pancreatic Cancer**
F. PYGOTT. *British Journal of Radiology* [*Brit. J. Radiol.*] **144**, 656–666, Nov., 1950. 15 figs., 13 refs.

In the last 4 years 29 men and 13 women have been admitted to the Central Middlesex Hospital with proved carcinoma of the pancreas; in 25 of these cases a barium-

meal examination was performed which in 16 cases showed some abnormality in the small intestine. In 5 of the 9 cases without positive *x*-ray findings only the head of the pancreas was involved. In one of these cases and in the remaining 4, in which the whole pancreas was involved, there was a large mass.

Clinical details of the 16 cases with positive *x*-ray findings are given [and should be read in the original by those interested]. The radiological findings included obstruction of the pylorus, obstruction of the duodenal loop, a large duodenal ulcer (apparently secondary to the pancreatic neoplasm), and enlargement or displacement of the duodenal loop and stomach. After reviewing the literature the author concludes that even slender *x*-ray evidence, in combination with the clinical history, may sometimes lead to a correct diagnosis of carcinoma of the pancreas at a usefully early stage.

Denys Jennings

1861. **Roentgenographic Findings in Schönlein–Henoch's Purpura. A Case Report**
J. S. FETTER and W. L. MILLS. *Radiology* [*Radiology*] **55**, 545–547, Oct., 1950. 4 figs., 9 refs.

A case of Schönlein–Henoch's purpura with partial obstruction of the third portion of the duodenum and an irregular appearance of the small bowel has been presented. Follow-up examinations over a three-month period showed return of the small bowel to normal and disappearance of symptoms. These small bowel changes were demonstrated roentgenologically.—[Authors' summary.]

1862. **Small Intestine Abnormalities in Anaphylactoid Purpura. Report of Two Cases**
J. J. ESPOSITO. *Radiology* [*Radiology*] **55**, 548–552, Oct., 1950. 4 figs., 7 refs.

Two cases of anaphylactoid purpura or Schönlein–Henoch's purpura are presented. Both patients showed marked abnormalities of the small intestine on roentgen examination. These changes are attributed to haemorrhages into the mucosal layer of the intestine and possibly into the mesentery. In each case the roentgen changes preceded the appearance of purpuric skin eruptions. After the subsidence of symptoms the roentgen abnormalities also disappeared.—[Author's summary.]

1863. **Early Roentgenological Evaluation in Patients with Upper Gastrointestinal Hemorrhage. Report of 58 Cases**
R. A. ELMER, A. A. ROUSUCK, and J. M. RYAN. *Gastroenterology* [*Gastroenterology*] **16**, 552–565, Nov., 1950. 8 figs., 10 refs.

This consecutive series of patients consisted of 36 severe cases and 22 moderately severe ones. The definition of severity was the presence of true shock or an erythrocyte count of less than 3,000,000 per c.mm. *X*-ray examination was performed 24 to 72 hours after admission and repeated after 10 to 14 days with a meal consisting of equal parts of barium sulphate and water thickened with " petrolagar " to the consistency of heavy cream. The meal was sucked up by the patient through a glass feeding tube. The oesophagus was examined with the patient supine and the right side propped up towards the screen, in the usual left anterior oblique position. The duodenal cap was filled by rotating the patient on to his right side. The usual left anterior oblique serial films were then taken after rotating the patient back to his original position.

A duodenal ulcer was diagnosed in 23 patients, but in 6 of them a lesion could no longer be demonstrated at the second examination 2 to 3 weeks later. In 8 out of 10 patients with a gastric ulcer the diagnosis was verified; the remaining 2 discharged themselves. Oesophageal varices were diagnosed in 6 cases, but in the only case where varices were found at necropsy the *x*-ray diagnosis was negative. Two patients had a hiatal hernia and 2 had neoplastic ulcers. Gastritis was diagnosed twice and no lesion was found in 14 patients. No lesion was found at the second examination which had been missed at the first.

[As in other American papers on this topic the dangers of early radiology are dismissed. The possibility of a non-existent lesion being diagnosed is not mentioned. In Britain the common practical problem is to exclude a chronic gastric ulcer and the abstracter believes that in the very ill patient gastroscopy is probably safer, less unpleasant, and more reliable than radiology for this purpose.] *Denys Jennings*

1864. **Roentgenological Diagnosis of Sponge in the Abdomen**
M. SLATER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 781–784, Nov., 1950. 5 figs., 4 refs.

A case is reported in which a radiological diagnosis of " sponge in the abdomen " was made, and subsequently verified at operation. The diagnosis was based on the persistence of a small localized collection of air bubbles, trapped in the mesh of the sponge, which did not shift when the position of the patient was changed, and was still present on repeated examination. The bubbles were small and more uniform in size than those of intestinal gas, and were not surrounded by a limiting membrane.

A. Orley

1865. **Anomalies of the Lumbosacral Vertebrae in Five Hundred and Fifty Individuals without Symptoms Referable to the Low Back**
J. D. SOUTHWORTH and S. R. BERSACK. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 624–634, Oct., 1950. 3 figs., 13 refs.

The authors review the radiological findings in the lumbar spine of 550 patients referred for barium-meal examination at the Mt. Alto Veterans Hospital, Washington, D.C., in order to assess the clinical significance of the common variations found in this region.

The length and width of the transverse processes of the lower lumbar vertebrae were measured. The maximum width for those of L4 and L5 were found to be 14 and 19 mm. respectively, values exceeding 19 mm. for L5 being considered to indicate an attempt at sacralization. L4 could be identified by the fact that its transverse

processes were smaller and more sharply angulated upward than those of L3. Asymmetry of the planes of the posterior articular facets between L4 and L5 and L5 and S1 was found in 36·4% of subjects. As none of these complained of symptoms it is concluded that such asymmetry, though mechanically undesirable, is not necessarily significant.

Some degree of spina bifida occulta occurred in 18·2% of subjects, but the incidence of scoliosis was no higher in these cases than in the rest of the series. In 6·4% of subjects there was evidence of sacralization of L5 in the form of grossly overdeveloped and wing-shaped transverse processes. Lumbarization of S1 was found in 2%, and first lumbar ribs in 11·3%. The incidence of osteo-arthritis appeared to be mainly related to age, but was slightly more frequent in patients with scoliosis. It was found rather often between the contiguous margins of the sacrum and sacralized transverse processes of L5. Otherwise the condition did not appear to be associated with congenital anomalies. *J. A. Shiers*

1866. **Urethro-cystography after Prostatectomy by Millin's Method.** (Studio uretrocistografico nei prostatectomizzati secondo il methodo di Millin)
P. Biondetti and A. Plotegher. *Annali di Radiologia Diagnostica* [*Ann. Radiol. diagnost.*] **22**, 299–307, 1950. 9 figs., 8 refs.

The authors report their radiological findings in 24 patients who had undergone prostatectomy by the extravesical, retropubic technique of Millin. Each patient was radiographed one month, and again 6 months, after the operation, this interval being considered sufficient to enable a large degree of stability of post-operative appearances to be attained. Retrograde urethrography, the contrast medium being tepid 30% barium suspension, was carried out in all cases, and those patients who were able to empty their bladder while lying on the radiographic couch (20 out of 24 cases) were also examined by means of intravenous urography, (This proportion is high compared with untreated patients suffering from prostatic carcinoma (24 out of 54), or from prostatic adenoma (13 out of 65 cases)). The authors describe their technique, the bladder and urethra being studied while the patient endeavours to hold urine, thus enabling the function of the striated sphincter of the urethra to be assessed. Antero-posterior and oblique projections are usually employed, the latter being more satisfactory because they show the whole length of the urethra.

The radiological appearances are described as follows: After the operation the bladder preserved its normal shape in all but a few cases in which the vertical axis was increased in length, and its contours remained normal except in one case in which radiographs taken one month after operation showed the presence of pseudo-diverticula; these diverticula had disappeared at 6 months. In one case there was evidence of ureteric reflux, which had probably been present before the operation. One month after the operation there was communication between the neck of the bladder and the prostatic bed, the contours of which were regular (except in 3 cases in which the posterior part of the neck of the bladder was resected). The size of the neck of the bladder depended in all cases on the size of the excised prostate and on the efficiency of the internal sphincter. Six months after the operation there was evidence of marked reduction in size of the neck of the bladder, due partly to scarring and partly to the recovery, in greater or less degree, of the tone of the internal sphincter, complete closure of the neck of bladder being demonstrated by retrograde urethrography, whereas on intravenous urography the neck of the bladder remained open.

The prostatic bed one month after the operation remained large, and was ovoid or pyriform in shape. Five months later some reduction in size was evident. In 3 cases in which the operation had been performed for carcinoma the outline of prostatic bed was irregular, serrated, and rigid, with somewhat defective filling, but in another case the contours were perfectly regular. Similarly in non-malignant cases the prostatic bed was sometimes regular and sometimes irregular, the post-operative appearances thus giving no clue to the nature of the previous prostatic lesion. The function of the external sphincter was in all cases well preserved, retrograde urethrography showing that the membranous part of urethra was well contracted when the patient tried hard to hold urine, whereas intravenous urography showed it to open, allowing free flow of the contrast medium, on micturition. While the external sphincter was contracted the prostatic bed was also reduced in size and its margins irregular. Only in 2 cases were the authors able to outline the vesiculae seminales.
L. G. Capra

1867. **Clinical Cinefluorography**
R. F. Rushmer, R. S. Bark, and J. A. Hendron. *Radiology* [*Radiology*] **55**, 588–592, Oct., 1950. 2 figs., 14 refs.

The effect of prolonged exposure to radiation on the patient is the primary factor which limits the duration of a cineradiographic recording. An arbitrary value of 20 r has been accepted as the maximum safe dose. However, as the shutter in most motion-picture cameras is closed approximately half of the time, interruption of the *x*-ray exposure during the closure of the camera shutter will permit the recording time to be doubled.

To achieve this, synchronization of *x*-ray tube and camera shutter is achieved, in the apparatus described, by means of a commutator attached to the shaft driving the advancing mechanism of the camera, the commutator being adjusted to close a circuit only while the camera shutter is open. This circuit activates a heavy-duty electronic switch which controls the flow of the current to the *x*-ray generator. With this mechanism each frame is exposed to light generated by four pulses of *x* rays and the flow of the current is interrupted during the next four pulses while the film is advanced. Details of the apparatus and of the electrical and *x*-ray circuits are given and illustrated. *A. Orley*

See also *Abstracts of World Surgery*, 1951, **9**, 242; 244; and 248.

Pathology

EXPERIMENTAL

1868. **An Experimental Study of the Role of the Adventitia in the Origin of Arteritis.** (Le rôle de l'adventice dans la genèse des artérites. Étude expérimentale)
R. LAPLANE. *Annales de Médecine* [*Ann. Méd.*] **51**, 397–444, 1950. 22 figs., bibliography.

The injection of irritants (bacterial toxins, metallic salts, or croton oil) into the adventitia of main arteries in various experimental animals was followed in about 50% by intimal and medial changes. These, in order of severity, were swelling and proliferation of endothelium, oedema, and then proliferation of the intimal tissues with or without involvement of the internal elastica; the intimal growth was sometimes enough to obliterate the lumen. In the media, where changes were less common and usually, although not always, associated with an intimal lesion, there occurred in order of severity, oedema, degenerative change in muscle and elastica, and even necrosis, which might be haemorrhagic with complete disappearance of the elastica. Lamp black was injected along with the irritant and never went beyond the outer layer of the media. Further, there was no evidence of spreading inflammatory reaction and in some of the animals the intima showed changes when the media did not. The author therefore concludes that the arteritis is not due to a direct action on the part of the irritant. He suggests that the injections produce " a sort of vasomotor anarchy " and may act either by inducing a spasm of the vasa vasorum or through an action on the tone of the main vessel, which may be manifest either as spasm or dilatation. (This last suggestion conflicts with the mechanism described by Leriche—sympathetic irritation, spasm, and then arteritis.) A third possible mechanism is a direct trophic upset consequent on the adventitial damage. The author finally discusses the various arteritic and obliterative changes met in clinical practice.

A. C. Lendrum

1869. **Hypercholesterolaemia in Starving Animals.** (О гиперхолестреинемии у голодающих животных)
S. V. NEDZVETSKI and A. S. DUBOVA. Архив Патологии (*Arkh. Patol.*] **12**, No. 5, 34–38, 1950. 11 refs.

Starvation hypercholesterolaemia was induced in dogs and rabbits. In agreement with previous observations, cholesterol metabolism was found to be much more stable in dogs, and the results of experimental cholesterolaemia in them were therefore more uncertain. Cholesterolaemia is a specific reaction, and the level of phosphorus-containing lipoids was not affected by starvation. It was, however, invariably associated with ketosis. When the level of ketosis could be lowered by the administration of glucose or of insulin, the level of blood cholesterol was also correspondingly depressed.

L. Crome

1870. **Electron-microscopic Examination of Human Milk Particularly from Women having Family Record of Breast Cancer**
L. CROSS, A. E. GESSLER, and K. S. MCCARTY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 270–276, Oct., 1950. 7 figs., 14 refs.

Milk obtained from nursing mice known to carry the mammary tumour agent (Bittner's milk factor) has been found to contain minute spherical particles with diameters varying from 20 to 200 mμ. It has been suggested that these particles represent the mouse mammary carcinoma virus. In view of the possibility that human and mouse breast cancer may have a similar aetiology, samples of human milk have been examined by electron microscopy for virus-like particles.

Ten samples of milk obtained from young, healthy, nursing women whose sisters, mothers, or grandmothers had suffered from breast cancer were found to contain spherical particles (20 to 200 mμ in diameter) with a smooth surface and a high density to the electron beam. In some instances they were grouped in pairs or clusters. They were particularly numerous in half of the samples examined. As a control, an examination was made of 32 samples of milk collected from young, healthy, nursing women with no recorded case of malignant tumour in their family in the two preceding generations. In eleven cases minute spherical particles were observed. Of the remaining 21 samples, 17 contained only occasional isolated, single particles and in the other 4 none was detectable.

The authors do not consider their results to justify any conclusions being drawn as to whether these minute particles are " associated with the hypothetical cancer agent ".

R. J. Ludford

1871. **Studies on Healing Processes in Malignant Tumours.** (Experimentelle Studien über Heilungsvorgänge bei bösartigen Geschwülsten)
C. HACKMANN. *Zeitschrift für Krebsforschung* [*Z. Krebsforsch.*] **57**, 164–190, 1950. 22 figs., 55 refs.

From a review of the literature concerning the resistance of tissues to malignant growth, and especially to metastasis, the author concludes that the evidence for the alleged spontaneous regression of primary malignant tumours in man and animals, except in the case of skin tumours, is unsatisfactory. There is good evidence, however, that embolic deposits of growth in lungs and lymph nodes are often absorbed. Two series of experiments are described, in the first of which tumours arising spontaneously in mice were excised, minced, suspended in saline, and injected subcutaneously or intravenously into the mice from which they had been removed; in 9 out of 17 cases no further tumours resulted. In the second series, the injection of sus-

pensions of Brown–Pearce tumour intravenously or intratesticularly into rabbits gave rise to widespread metastases, with early death. When injected subcutaneously, or into the conjunctiva or anterior chamber of the eye, however, it grew locally only, and often regressed. Histological examination of regressing grafts showed haemorrhages and progressive necrosis spreading outwards from the centre, fibrosis, and resorbtion. Tumour tissue around the blood vessels survived longest.

The author concludes that ischaemia, resulting from capillary damage which may be a form of sensitization reaction to the tumour, is mainly responsible for regression. He found no evidence that cellular or humoral immunity plays a significant part. *M. H. Salaman*

1872. **Isolation of Fungi from Transplanted Chemically Induced and Spontaneous Tumours. 1. General Considerations**

I. C. DILLER and M. FISHER. *Cancer Research* [*Cancer Res.*] **10**, 595–603, Oct., 1950. 10 figs., bibliography.

Fungi were seen in smears of human and mouse tumours examined by various cytological techniques and were isolated by culture on Sabouraud's agar or Littman's ox-gall agar. The mouse tumour tissues included transplantable carcinoma and sarcoma, tumours induced by methylcholanthrene, spontaneous mammary carcinoma, and lymphatic leukaemia. The human tumour tissue was biopsy material from patients undergoing chemotherapy, and was mainly from mammary carcinoma and enlarged lymph nodes in cases of Hodgkin's disease or lymphosarcoma. Fungi were isolated from all spontaneous and chemically-induced tumours and from all but a few of the untreated transplanted tumours of mice; they included *Syncephalastrum*, *Alternaria*, imperfect fungi, and yeast-like species. The fungi isolated from human tumours all belonged to the group of imperfect fungi and seemed to be allied to the blastomycetes. Spore suspensions of *Syncephalastrum* and *Alternaria*, when freshly isolated from tumours, were pathogenic for mice; intraperitoneal or intramuscular injections killed mice within 4 days.

At the present stage the authors are not prepared to attempt any explanation of the presence or role of fungi in tumour tissue, but in view of their successful isolation from so many types of neoplasms, including human tumours and spontaneous tumours of mice, they are convinced that the fungi must play some significant part, if only a secondary one. *L. Foulds*

1873. **The Transplantation of Liver Tissue.** (Über Transplantation von Lebergewebe)

E. KNAKE. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **319**, 321–330, 1950. 5 figs., 13 refs.

Free transplants are compared with tissue slices as a means of estimation of tissue metabolism, the object in both instances being to preserve viability of all parts of the tissue. If tissue sections are thick, only a more or less extensive cortical area will take part in metabolism because of the slowness of diffusion, while the core of the section will remain inert. The thinner the tissue section the shorter is the path of diffusion and the smaller the area of inert tissue. With a certain thickness of section, termed the " critical section thickness " (*Grenzschnittdicke*) there is no inert area; this critical section thickness varies with, among other factors, the metabolic rate of the individual tissue and the rate of diffusion of the constituents of the nutrient medium; in free transplants the critical tissue thickness depends on the distance between the transplanted cells and the nearest capillary.

Working at the Kaiser Wilhelm Institute for Cellular Physiology in Berlin, the author transplanted sections from the liver of laboratory animals [it is not stated what animals were used] into the lesser omentum and mesotestis. The dimensions of the transplants were, on the average, 4 mm. × 1·5 mm. × 1·5 mm. At intervals of from 2 to 20 weeks the animals were killed and the transplants examined under the microscope. They were found to have " taken " without any reaction in, or demarcation from, the host tissue. The liver cells retained their original appearance and differentiation for at least 20 weeks; in all transplants mitoses in liver cells were seen, and frequently binuclear cells. The author ascribes these good results to the employment of autotransplantation as distinct from homo-transplantation, the use of thin sections and aseptic technique, and the choice of a vascular reception area. *N. Alders*

1874. **Further Investigation on the Effect of Vitamin B_{12} Concentrate upon Hepatic Injury Produced by Carbon Tetrachloride**

D. KOCH-WESTER, P. B. SZANTO, E. FARBER, and H. POPPER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 694–704, Nov., 1950. 9 figs., 23 refs.

Previous work having indicated that large doses of vitamin B_{12} exerted a protective effect on the liver against injury caused by carbon tetrachloride (CCl_4), the authors carried out further experiments designed to investigate this effect. Female rats, 2 to 4 months old, were used. To one set of 4 groups of animals, 15, 10, 2·5, and 1·0 μg. respectively of vitamin B_{12} per 100 g. body weight was administered by subcutaneous injection on 4 consecutive days. Simultaneously with the last dose, 0·033 ml. of CCl_4 (in 1 ml. of mineral oil) per 100 g. was injected intraperitoneally. To another set of 2 groups of animals 30 and 15 μg. respectively of vitamin B_{12} per 100 g. was administered 6, 12, 24, and 36 hours after the same dose of CCl_4. Control animals were given either the same dose of CCl_4 without vitamin B_{12}, or nothing. The animals were killed 48 hours after the administration of CCl_4. Bromsulphalein retention was estimated just before death, 30 minutes after the intraperitoneal injection of 5 mg. of the dye per 100 g. Liver weight at necropsy was compared with the body weight at the time of injection of the CCl_4. The total liver lipid content was also estimated and histological examinations made. Additional biochemical analyses were carried out on four other groups of animals receiving respectively: 15 μg. of vitamin B_{12} per 100 g. in 4 daily doses; 0·033 ml. of CCl_4 per 100 g. intraperitoneally;

the same amounts of vitamin B_{12} given before CCl_4 administration; and nothing. In these animals estimations were made of the liver alkaline-phosphatase, esterase, total nitrogen, total nucleic acid, and pentose nucleic acid content.

The results of these experiments are clearly set out in tables and excellent photomicrographs. It was found that the lethal dose of CCl_4 was significantly increased by the previous injection of vitamin B_{12}. The changes produced by CCl_4 in the absence of the vitamin were not entirely prevented by its previous administration; bromsulphalein retention was less, however, and there was less increase in liver protein and lipid content, a smaller rise in alkaline-phosphatase activity, and a smaller decrease in esterase content. Histologically there was considerable reduction in fatty change and central necrosis, and loss of pyroninophilia was less than in untreated rats. (Popper *et al.*, *Proc. Soc. exp. Biol., N.Y.*, 1949, **71**, 688.)

The authors conclude that the previous administration of vitamin B_{12} is effective in modifying the toxic effect of carbon tetrachloride on the liver. The explanation of this action is not clear, but is probably pharmacological and related to the vasodilator action of the vitamin.

B. G. Maegraith

1875. **Effect of a Spleen Extract on Experimentally Produced Liver Fibrosis with Macrocytosis.** (In English] L. GOLDBERG, G. HAMMARSTEN, O. HELLSTRÖM, G. LINDGREN, and C. M. PLUM. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] Suppl. 77, **22**, 1–75, 1950. 37 figs., 35 refs.

1876. **Diabetes and Pregnancy. An Animal Study.** [In English]
G. T. HULTQUIST. *Acta Pathologica et Microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **27**, 695–719, 1950. 5 figs., 40 refs.

The pancreas was removed at varying stages of pregnancy from 204 rats: 83 died immediately or soon afterwards, the mortality being higher the later in pregnancy the operation was performed. In all, 46 rats aborted at various times, while 66 reached full term and 4 others nearly did so; the risk of abortion was greater the earlier in pregnancy pancreatectomy was performed. Pregnancy occurred again in 9 of the rats, in 2 more than once, and in 4 out of 6 non-pregnant pancreatectomized rats. There was a significant increase in birth weight in the offspring, the mean weight of the young being closely correlated with the weight of the mother, but not with the number in the litter. The highest incidence of increased birth weight was in the offspring of the rats pancreatectomized on the 8th to 12th day and treated with insulin and a uniform diet; 81% of these offspring were stillborn. The high birth weight was not due to increase of fat, but to general enlargement with increase in length and splanchnomegaly; in a few cases oedema was also present.

The mean duration of pregnancy was 22·6 days in the pancreatectomized animals as against 21·7 days in the controls, the increase being considered significant. Glycosuria in the mothers rose slightly after pancreatectomy, but fell again immediately before delivery; the hyperglycaemia was less affected and the general condition often deteriorated, sometimes with ketosis. After delivery hyperglycaemia and glycosuria increased, but the general condition improved and ketonuria was not observed. Blood sugar level in the offspring followed that in the mother, but at a slightly lower level. Glycosuria and ketonuria were less the later in pregnancy pancreatectomy was performed.

In the giant young there was enlargement of the adrenal cortex, testes, and parathyroids and to a lesser extent of the islets of Langerhans and the thymus, and there was an increase in chromophilia in the anterior pituitary. In the normal-sized offspring there was no significant enlargement of the islets and in general less marked changes in the endocrine organs. As giant growth occurred only in the offspring of diabetic mothers, it was felt that it might be due to endocrine influences in the mother, though it could not be related to the degree of islet hyperplasia or to the insulin treatment of the mothers.

The author points out the close resemblances of their findings to those in diabetic human mothers and their children.

Robert de Mowbray

MORBID ANATOMY

1877. **Endocrine Gland Changes in Plasmacytoma.** (Inkretdrüsenveränderungen bei Plasmocytom)
J. SMEREKER. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **319**, 72–80, 1950. 5 figs., 20 refs.

From histological examination of the ductless glands, especially pituitary and adrenals, in persons with plasma-cell myelomatosis, the conclusion is reached that this disease is preceded by a primary disorder of protein metabolism, due to nervous and endocrine disturbances, and that the plasma-cell neoplasia is a secondary consequence of this. [In the abstracter's opinion, the evidence advanced is inadequate to sustain this speculative idea.]

R. A. Willis

1878. **Lesions Resembling Boeck's Sarcoid in Lymph Nodes Draining an Area Containing a Malignant Neoplasm** E. M. NADEL and L. V. ACKERMAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 952–957, Oct., 1950. 5 figs., 21 refs.

Lymph nodes removed from the neighbourhood of 5 malignant tumours were found on histological examination to contain lesions indistinguishable from those of Boeck's sarcoid. The primary growths were situated in breast, soft palate, forehead, ampulla of Vater, and bronchus, and the nodes involved in each case were those which drained the malignant area. There was no evidence of systemic sarcoidosis in any of the 5 patients.

It is suggested that local sarcoidosis is a non-specific type of tissue reaction peculiar to certain individuals, and that the "pattern" of the host's response is of more significance than the exciting cause.

G. B. Forbes

1879. **Changes in the Human Brain in Chronic and Acute General Anoxia.** (Veränderungen des menschlichen Gehirns bei chronischem und akutem allgemeinem Sauerstoffmangel)
H. PLAMBECK. *Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie* [*Beitr. path. Anat.*] **3**, 77–94, 1950. 4 figs., 43 refs.

The brain was examined in 5 cases of chronic cerebral anoxia resulting from anaemia due to leukaemia, carcinomatosis, or haemorrhage, or from chronic heart failure. No morphological changes were demonstrated on histological examination. The brain was also examined in 5 cases of acute anoxia due to short-lived cardiac arrest or sudden extensive haemorrhage. In 2 cases in the former group there were widely scattered areas of ischaemic degeneration of ganglion cells of the 3rd and 5th cortical layers. In one of the 5 cases in the latter group necrosis of putamen and globus pallidus was demonstrated. The remaining 2 cases in this group displayed similar degenerative changes of cortical ganglion cells, with chromatolysis of erratic distribution. *R. Salm*

1880. **Changes in the Thyroid Gland in Chronic Malnutrition and in Starvation.** (Veränderungen der Schilddrüse bei chronischer Unterernährung und im Hunger)
W. MÄHRLEIN. *Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie* [*Beitr. path. Anat.*] **3**, 13–23, 1950. 3 figs., 35 refs.

The thyroid gland was examined in 71 patients dying of inanition or cachexia owing to carcinoma or tuberculosis. The loss of weight of the organ varied from one-third to one-half of the normal average. Histologically the epithelium was mostly cuboidal or flat, the colloid frequently stained poorly and with a purple hue and showed a concentric arrangement, while the stroma was present in increased amounts, occasionally to such an extent as to cause collapse of follicles and atrophy. Lymphocytic infiltration was also in evidence. The author distinguishes three types of change: an inactive gland, simple atrophy, and atrophy combined with sclerosis. *R. Salm*

1881. **The Minute Anatomy of the Blood Supply of the Thyroid in Various Types of Goitre.** (La minuta vascolarizzazione della tiroide nei vari tipi di gozzo)
B. AMISTANI. *Archivio Italiano di Anatomia e Istologia Patologica* [*Arch. ital. Anat. Istol. pat.*] **23**, 365–375, 1950. 5 figs., 19 refs.

It is a basic physiological principle that the more active an organ the greater is its blood supply, and this is particularly true in the case of the glands of internal secretion. The thyroid gland is no exception, but whereas the details of its macroscopic blood supply from the thyroid arteries and their anastomoses are generally well known, the microscopical details may be less so. Of the many suggested classifications of this minute anatomy, that of Major (1909) is the simplest and is as follows. The main branches of the thyroid vessels run underneath the capsule and from these spring the interlobular arteries, which in turn give rise to the intralobular branches; from these originate the follicular vessels, which give rise to the extensive capillary anastomoses which surround each follicle. The histological examination of the thyroid gland shows, besides, one or more of three types of follicle, large, medium, and small, these last often being completely devoid of colloid; the larger and fuller the follicles, the less active the gland.

The author studied 30 diseased thyroids which had been removed surgically, 7 being of the parenchymatous, 10 colloid, 7 cystic, and 6 of the exophthalmic type of goitre. In parenchymatous goitres the follicles were small, with little or no colloid, and with cubo-cylindrical epithelium and little surrounding connective tissue. The capillaries, tortuous and varicose and ranging in calibre from 5 to 10 μg., were forming a close network so indistinct and irregular that its various constituents could not readily be made out. In the colloid goitres the follicles were large and full and the epithelium was flattened, and the perifollicular capillaries formed a wider net in which the various constituents could be distinguished easily: though tortuous, they were not varicose, and their calibre varied from 5 to 14 μ. In cystic goitre the follicles were as in the preceding type, but the capillary net was wider and the calibre of the capillaries lay between 5 and 16 μ. In exophthalmic goitre the follicles were very small and empty, or nearly so, but their epithelial cells were columnar and very numerous. The capillary arrangement resembled that of the parenchymatous type, but the vessels were even more numerous and they formed a closer net. Their calibre varied from 4 to 8 μ.
S. M. Vassallo

1882. **Parietal Endocarditis of the Left Auricle.** (Sull'endocardite parietale atriale sinistra)
M. A. DINA. *Archivio Italiano di Anatomia e Istologia Patologica* [*Arch. ital. Anat. Istol. pat.*] **23**, 416–458, 1950. 25 figs., bibliography.

A type of endocarditis of the left atrium is described. It is characterized by a rugose thickening of the endocardium which may be diffuse or patchy, pinkish grey or white in colour, and without deposition of fibrin. The condition was first described by McCallum (*Bull. Johns Hopk. Hosp.*, 1924, **35**, 329).

The author describes 5 cases in patients aged from 18 months to 42 years. The disease was febrile, running an acute or subacute course ending in cardiac insufficiency; sometimes articular rheumatism occurred, sometimes pericarditis and pleuromediastinitis. Histologically the lesions showed fibrinoid degeneration, fibroblastic proliferation of the subendothelial tissue sometimes producing nodular projections on the surface of the endocardium, and scanty evidence of exudation. Aschoff nodes were present in every case. In none was the endothelium damaged. One patient had a fibrosed mitral valve and another a verrucose lesion of the mitral valve.

The extensive recent literature on endocarditis is discussed and the view is taken that in man the different types form a continuous series, with rheumatic endocarditis at one extreme and acute bacterial endocarditis at the other. Fibroplastic endocarditis, the eosinophilic

type of Löffler, the verrucose type of Libmann–Sacks, and endocarditis lenta are intermediate conditions in the series. This is the conception of Klinge, septic endocarditis being an anergic phase and rheumatic endocarditis a hyperergic phase.

Endocarditis of the left atrium falls into the series alongside the rheumatic and Löffler's types of endocarditis, the tissue resistance being high and the virulence of the infecting agent low. *F. A. Langley*

1883. **Primary Reticulosarcoma of the Heart.** (Reticolosarcoma primitivo del cuore)
G. DAGNINI. *Archivio Italiano di Anatomia e Istologia Patologica* [*Arch. ital. Anat. Istol. pat.*] **23**, 470–482, 1950. 6 figs., 24 refs.

A primary tumour of the heart in a woman of 56 is described. She was admitted to hospital with marked dyspnoea, orthopnoea, cyanosis, and moderate oedema of the sacrum. On examination there was moderate pulmonary congestion, with increased cardiac dullness and a heart rate of 44. The electrocardiogram showed complete atrio-ventricular block. She died in a Stokes–Adams attack. At necropsy a tumour was found in the posterior part of the heart invading the right atrium and right ventricle and invading the septum. Histologically the tumour was a reticulosarcoma.

The literature is briefly reviewed. Since 1865, 88 primary mesenchymal tumours of the heart have been described, including round-cell (19), spindle-cell (17), polymorphic (10), and giant-cell sarcomata (5), fibrosarcoma (8), rhabdomyosarcoma (7), myxosarcoma (5), leiomyosarcoma (4), angiosarcoma (3), lymphosarcoma (2), embryonic sarcoma (2), melanotic sarcoma (1), fibromyxosarcoma (1), and 3 which were unclassified. The author claims that his case is the first tumour of the reticulo-endothelial system to be reported in the heart. [This seems unlikely, since some of the earlier primary tumours might quite well have fallen into this group; the author has not examined the previous reports critically enough and in sufficient detail to make this claim.] *F. A. Langley*

1884. **The Development of Atheromatous Changes in the Aorta.** (О развитии атеросклеротических изменений аорты)
T. N. KHAVKIN. Архив Патологии [*Arkh. Patol.*] **12**, No. 5, 23–33, 1950. 7 figs., 30 refs.

The author has studied the histogenesis of atheroma in human and experimental material. He found that some hitherto obscure changes could best be observed in sections cut along the plane of the aortic intima. The investigation confirmed the previous general conclusions of Anitchkov and his school that cholesterol, together with some proteins, reaches the subendothelial tissues of the intima by seepage from the blood stream. The xanthomatous cells are then formed *in situ* by the phagocytosis of the lipoid, chiefly by the polyblastic cells which are normally present in the intima and partly, perhaps, by wandering cells reaching the atheromatous plaque from the blood. The endothelial cells of the intima do not take part in this phagocytosis, nor is there any evidence to support the view of Leary that the lipoid macrophages are formed in some extra-mural locations of the reticulo-endothelial system. The lipoid is first deposited in the interstitial substance of the intima and is then absorbed by cells. These cells are, as stated above, chiefly polyblasts in the larger foci. In the small plaques macrophages are, however, formed from the so-called Langhans cells. The lipoid may become extracellular again later, when the phagocytic cells die; but this process is inconsiderable in quantity and late in occurrence. During the reversal of atheromatosis, fat disappears initially from the interstitial tissue and later from the subendothelial fixed cells. It is retained longest in the polyblasts. *L. Crome*

1885. **Myocardial Lesions in Progressive Muscular Dystrophy**
W. G. NOTHACKER and M. G. NETSKY. *Archives of Pathology* [*Arch. Path.*] **50**, 578–590, Nov., 1950. 9 figs., 6 refs.

Eleven cases of progressive muscular dystrophy were found in nearly 9,000 necropsies. Of these cases, 6 showed myocardial lesions which are here described. All the patients were males and in all but one the onset of the disease was before the age of 8 years. A family history of muscular dystrophy was obtained in 4 cases. Two of the patients had had transient cardiac irregularities, but the other patients had neither signs nor symptoms of heart disease. The duration and severity of the lesions in the skeletal muscles appeared to bear no relation to the severity of the myocardial lesions.

The authors give the following description of the myocardial lesions in progressive muscular dystrophy: "The epicardium is usually normal. The coronary arteries are not implicated, but a few small atheromatous plaques may be present. The myocardium either is scarred in an irregular, patchy manner or is diffusely yellow-brown. The ventricular endocardium may be slightly thickened. The valves are not involved. Throughout the myocardium there are areas of scarring which tend to divide the muscle fibres into individual fasiculi and muscle fibres are present singly or in groups within many of the scars. The entrapped muscle fibres undergo various changes: vacuolation, fragmentation, hypertrophy, shrinkage and phagocytosis. Isolated muscle fibres with similar changes are found in the better preserved portions of the myocardium. The fat content of the scars is variable. There is oedema of the stroma of the unscarred myocardium, with an occasional lymphocyte or macrophage between the separated collagen fibres." *R. B. Lucas*

1886. **The Problem of Myocardial Fragmentation.** (К вопросу о фрагментации миокарда)
R. G. KUTSENKO and M. B. GANESHINA. Архив Патологии [*Arkh. Patol.*] **12**, No. 5, 65–71, 1950. 21 refs.

The significance of the fragmentation of the heart muscle seen in histological sections is not yet fully understood. In this series heart muscle was kept for varying periods up to 5 days at room temperature

before being treated with different fixatives and then examined in the usual way. It was found that post-mortem autolysis and the nature of fixatives played no part in the production of fragmentation. It was most marked in the papillary and mural muscles of the left ventricle. The authors review the literature and discuss the possible aetiology of the condition. They consider that it is produced terminally, perhaps by ventricular fibrillation, and that the previous state of the heart muscle is an associated factor in its development.

L. Crome

1887. **The Pathology of the So-called Isolated Myocarditis and its Place among the Allergic Disorders of the Cardiovascular System.** (Патология так называемого изолированного миокардита и его место в ряду аллергических пораженнй сердечно-сосудистой системы)
Y. L. Rapoport. Архив Патологии [*Arkh. Patol.*] **12**, No. 5, 72–84, 1950. 6 figs., 18 refs.

The nosological position of isolated myocarditis is reviewed, and the author contributes his own observations in 12 cases of the condition. Two of them were in patients in whom isolated myocarditis had been diagnosed correctly in life and who subsequently recovered and died later from an unrelated cause. Morphologically, the condition may be classified into three main types: (1) an inflammatory-infiltrative type, in which the characteristic lesions consist of cellular exudate in the interstitial tissues of the heart; (2) a dystrophic (destructive) type characterized by foci of muscle necrosis; and (3) a mixed type. The restriction of the lesions to the heart, the prevalence of thrombosis, and hyperergic changes in blood vessels are constant features in this condition. Its aetiology is discussed and the author concludes that in the light of the present knowledge it must be regarded as an allergic complication of many different toxic or infective states, in which the initial cause had either completely disappeared or had been overshadowed by the involvement of the heart. There is therefore no reason, in principle, for separating it from the larger group of cases of myocarditis complicating other diseases, such as the fevers. Of incidental interest also was the finding, in one of the author's cases, of granulomata which were structurally identical with Aschoff's rheumatic nodes.

L. Crome

1888 (*a*). **Studies on Rigor Mortis. Part I. Observations on the Microscopic and Submicroscopic Structure**
R. D. Smith. *Anatomical Record* [*Anat. Rec.*] **108**, 185–197, Oct., 1950. 14 refs.

A microscopical study was made by the author, at the University of Maryland Medical School, Baltimore, of the changes occurring after death in the skeletal muscle of rats. The animals were killed by exsanguination, and the gastrocnemius removed and suspended in a moist chamber. After varying intervals post mortem, the muscle was fixed in Bouin's solution or 10% formalin, and paraffin sections made, some of these being treated with iron-haematoxylin and others being examined unstained.

Muscles fixed from 2 to 10 hours post mortem appeared histologically normal, both under normal and polarized light. In those fixed between 10 and 20 hours after death the more superficial fibres showed neither birefringence nor striation, and this appeared to be associated with bacterial action. The inner fibres showed evidence of minor degenerative changes in the form of localized isotropic areas. From 20 to 30 hours after death the changes were of the same type, but more extensive, and in the superficial part of the muscle were to be seen a number of discrete, optically very active areas (anisotropic granules). Between 30 and 50 hours post mortem the degeneration gradually became uniform throughout the muscle, although many central fibres showed a periodicity due to the appearance of a strongly negative birefringent material in the region of the I band.

It is suggested that the changes at the periphery of the muscle are due to bacterial action and those in the centre to autolysis. The anisotropic granules appear to be fragments of decomposed sarcomere constituents. The significance of the persistence of striations associated with changes in the I band is discussed; it is concluded that this is due to the unmasking of a lipoid in this region.

Peter Ring

1888 (*b*). **Studies on Rigor Mortis. Part II. Qualitative Observations on the Post Mortem Shortening of Muscles**
R. D. Smith. *Anatomical Record* [*Anat. Rec.*] **108**, 207–216, Oct., 1950. 2 figs., 14 refs.

The paired gastrocnemius muscles of adult rats which had been killed by exsanguination were mounted in muscle warming chambers, the proximal end remaining attached to the femur, which was fixed, and the severed tendo achillis connected to a lever recording on a kymograph moving at 4 mm. an hour. The changes in length were observed in muscles kept (1) at room temperature (25° C.), (2) at room temperature after tetanization, and (3) at 37° C. In muscles of group (1) there was often a period of slight lengthening, followed by contraction which was maximal after 8 hours, and then by slow lengthening again. In those kept at 37° C. the shortening was maximal after 4 hours. Tetanization before mounting had the effect of hastening the onset of shortening, there being no initial lengthening. From a comparison of the average curve of shortening with those of hardness, *p*H, elasticity, and heat production, it is concluded that the shortening process is a sensitive indicator of the post-mortem chemical changes in muscle, and is associated with the breakdown of adenosine tri-phosphate.

Peter Ring

CLINICAL PATHOLOGY

1889. **Cytologic Examination of Breast Secretions**
O. Saphir. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 1001–1010, Nov., 1950. 12 figs.

This investigation was undertaken to see if it might be possible to diagnose and to distinguish chronic cystic mastitis, papilloma, and intraductal carcinoma of the breast by studying discharges from the nipple.

In all three conditions were seen degenerated erythrocytes and phagocytes containing blood-pigment granules. In chronic cystic mastitis there were large phagocytes with relatively few epithelial cells derived from the duct. In intracystic papillomata were seen clumps of epithelial cells with oval, clear-cut, vesicular nuclei and well-outlined cytoplasm. There was neither anachromasia nor anaplasia. Intraductal carcinoma was characterized by the large size of the cells and their nuclei, irregular chromatin, clumps of chromatin within the nucleus, and the large nucleolus. The nuclear membranes were clear-cut, but the cell membranes were indistinct. Anaplasia and anachromasia were in evidence when the cells were found in clumps.

Examinations were made in 90 cases with the Papanicolaou technique: the secretion in 37 showed no abnormality, and in one was from an abscess, in 21 it was characteristic of chronic mastitis, in 13 of carcinoma, and in 7 of papilloma, in 5 it was considered suspicious of carcinoma (of these, 4 later proved to be carcinomatous), and in 6 the diagnosis was of possible papilloma. Carcinoma was diagnosed correctly 11 times; in 2 cases it was misdiagnosed as chronic mastitis, and in one as papilloma. In 2 instances chronic cystic mastitis was incorrectly diagnosed as carcinoma. Thus there were 2 false positive and 3 false negative cancer diagnoses in this series. The author concludes that the cytological examination of discharges from the nipple is destined to become an important adjuvant in the clinical diagnosis of certain breast lesions. *H. Lehmann*

1890. **A Micro-method for the Estimation of Glucose in Organic Fluids.** (Micro-méthode de dosage du glucose dans les liquides organiques)
P. CASTAIGNE. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4453–4458, Nov. 22, 1950. 2 figs., 7 refs.

1891. **Lung Function Studies. IV. Postural Changes in Respiratory Dead Space and Functional Residual Capacity**
W. S. FOWLER. *Journal of Clinical Pathology* [*J. clin. Path.*] **29**, 1437–1438, Nov., 1950. 6 refs.

Postural changes in functional residual capacity and respiratory dead space were measured in 5 male subjects. The functional residual capacity, respiratory dead space, and the average dead space/tidal volume fraction were greater when the subjects were sitting than when supine. Intermediate values were obtained in the semi-reclining position.—[Author's summary.]

1892. **Lung Function Studies. V. Respiratory Dead Space in Old Age and in Pulmonary Emphysema**
W. S. FOWLER. *Journal of Clinical Pathology* [*J. clin. Path.*] **29**, 1439–1444, Nov., 1950. 2 figs., 13 refs.

Continuous measurement was made of N_2 concentration and volume-flow of gas expired after O_2 inhalation. The graph of N_2 concentration plotted against volume expired during one expiration can be separated into three phases in which N_2 concentration successively (1) equals inspired concentration, (2) increases in an S-shaped fashion, (3) is rectilinear. Evidence has been presented previously that in normal subjects the completion of phase (2) indicates that the dead space has been washed out and phase (3) consists of alveolar gas. In certain records obtained during quiet breathing by patients with pulmonary disease, there was uncertainty whether phase (2) was completed. For measurement of respiratory dead space it is necessary that the dead space be washed out completely and an alveolar concentration be obtained.

The completion of phase (2) and presence of phase (3) were verified in studies on patients using maximal expirations following inspirations of O_2 alone, and a sequence of O_2 and air. These studies support the belief that completion of phase (2) indicates that the dead space has been washed out, and that phase (3) consists of alveolar gas; this permits the selection of a value for alveolar N_2 concentration which can be used in measurement of the respiratory dead space.

Ten normal young men, 11 normal old men, and 12 elderly male patients with marked pulmonary emphysema were studied in a semi-reclining position. Measurements were made of (*a*) respiratory dead space during quiet breathing and after maximal inspiration of O_2 and (*b*) tidal volume during breathing of O_2 and compressed air. Three patients, during inhalation of O_2, did not completely wash out the dead space on expiration. The mean respiratory dead space of 9 patients with emphysema, measured during quiet breathing, was 169 ml.; this was significantly greater than the mean value of 127 ml. for the young men. The mean value for old men was 150 ml. The respiratory dead space after maximal inspiration was similar in all three groups. The tidal volume of patients with emphysema and anoxemia was smaller when breathing O_2 then when breathing air. The significance of data dependent on the dead space/tidal volume fraction of patients with emphysema is discussed.—[Author's summary.]

1893 (*a*). **A New Test in Clinical Pathology. The Reticulo-endothelial Diagram.** (Un nouveau test physiopathologique: la fiche réticulo-endothéliale)
G. SANDOR and J. C. WEILL-FAGE. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1466–1470, Nov. 10, 1950. 2 figs.

In presenting this new test the authors believe that it will be very helpful in the diagnosis and prognosis of many diseases. The test is based on the demonstration of variations in serum euglobulin content, which are thought to reflect pathological changes in the reticulo-endothelial system (R.E.S.). Briefly, the technique consists in initial separation of the euglobulins by dialysis and the estimation of the fractions precipitated at various *p*H levels from 7·7 to 4·8, the nitrogen content of each precipitate being estimated by the Kjeldahl method. A curve is set up, the abscissae being *p*H values and ordinates the various fractions expressed as a proportion of the total serum euglobulin content. A normal curve was constructed from estimations on 12 normal subjects. It was found that the precipitates could be divided into 3 groups (I, II, and III) according to the *p*H range in which they were formed, each group being made up of several fractions (I_1, I_2, I_3, etc.). One precipitate formed

during the initial dialysis, I_1, had special characters and was considered separately.

Interpretation of the "diagram" depends upon a study of the curve obtained and the quantitative alterations in the euglobulins of fraction I_1. Four types of variation occur, corresponding to four different pathological groups: (1) An increase in proportion of euglobulin I_1 above the normal level of 0·6 part per 1,000, due to hyperplasia or hyperfunction of a particular part of the R.E.S. This is best observed in hepatic and portal system diseases such as epidemic jaundice, cirrhosis with jaundice, and typhoid fever in the convalescent stage. It is suggested that the change in euglobulin is due to a disturbance of the Kuppfer cells. (2) The curve is displaced to the alkaline side in conditions with moderate or marked hyperplasia of the R.E.S. such as is found in convalescent typhoid fever, polycythaemia, cholangitis, acute articular rheumatism, chronic polyarthritis, myxoedema, and multiple myeloma. (3) Displacement to the acid side occurs in conditions of hypoplasia and blockage of the R.E.S. such as chronic azotaemic and hypertensive nephritis, myocardial infarction, obstructive jaundice, and tuberculous meningitis. (4) Modifications chiefly affecting the group-III euglobulins occur in disturbances of lipid metabolism.

No relation exists between this test and the classical albumin : globulin ratio, nor does electrophoresis give any indication of the presence of abnormal euglobulins. The serum left after the elimination of these euglobulins gives a normal electrophoretic pattern. The authors suggest that an equilibrium normally exists between the various euglobulins, pathological variations in which are reflected quantitatively by their technique.

[Very little detail of the technique is given, but it would appear to need the resources of a well-equipped laboratory of chemical pathology.] *R. F. Jennison*

1893 (*b*). **A New Pathological Test in the Study of Liver Disease.** (Un nouveau test physio-pathologique appliqué à l'étude des maladies du foie)
R. CATTAN, G. SANDOR, and J. C. WEILL-FAGE. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1470–1473, Nov. 10, 1950. 3 figs.

In this second paper (see Abstract 1893 (*a*)) the authors describe the application of their test to the study of hepatic disorders. They performed the test in 6 cases of infective hepatitis, 5 cases of obstructive jaundice due to neoplasm, and 9 cases of cirrhosis. The curves obtained within each group were identical, and one representative case from each group is described, with details of other liver function tests. In the case of cirrhosis the curve falls well within the alkaline region, and the proportion of euglobulin fraction I_1 is always higher than 0·6 part per 1,000, being very high in cases with jaundice. In infective hepatitis the curve is only just in the alkaline region and tends to rejoin the normal curve at *p*H 6. The proportion of euglobulin I_1 is always increased, to about 0·8 part per 1,000. In obstructive jaundice the curve is shifted to the acid side and the amount of euglobulin I_1 is normal or diminished. It is proposed to make further studies of the euglobulins during the course of these diseases to see if any prognostic significance can be found. *R. F. Jennison*

1894. **Thermal Coagulability of Serum Proteins and the Diagnosis of Malignant Disease**
H. JACKSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1201–1203, Nov. 25, 1950. 2 figs., 5 refs.

The thermal coagulability of serum proteins in the presence of iodoacetic acid has been examined in 65 normal individuals, 89 cases of malignant disease, and 63 patients with other diseases.

An "iodoacetate index" has been calculated for each serum; this has been used to assess changes in the coagulability of serum proteins in relation to disease. The distribution pattern of the figures so obtained leads to the conclusion that the determination of such an index is useless in the diagnosis of malignant disease. Not only may serum from apparently healthy individuals furnish iodoacetate figures falling into the index range suggested for cancer cases, and vice versa, but most cases of non-malignant disease gave values in the "cancer range".

The test also reveals no consistent correlation between "iodoacetate index" and the severity of the malignant condition; even advanced cases of cancer may give figures in the "normal range".—[Author's summary]

1895. **Transparietal Needle Biopsy of Lung Tumours by Condorelli's Technique.** (La ponction-biopsie transpariétale des tumeurs du poumon par la technique de Condorelli)
A. CIONI. *Journal Français de Médecine et Chirurgie Thoracique* [*J. franc. Méd. Chir. thorac.*] **5**, 417–423, 1950. 8 figs.

The histology of lung tumours may be verified by bronchoscopic biopsy, by recovery of cells in sputum or aspirated material, or by transpleural puncture biopsy with a needle. If the first two methods prove unsatisfactory, the third may be resorted to, providing the tumour is within 2 or 3 cm. of the pleura. A 20-ml. syringe fitted with a needle of 1 or 1·5 mm. bore is filled with sterile physiological saline and all air expelled. The tumour is located radiologically and, while the patient holds his breath after an initial expiration, the needle is passed through the chest wall and lung into the growth, suction being maintained on the plunger throughout. After withdrawal, the material obtained is expelled into serum and fragments of tissue picked out, fixed, and stained for microscopical examination.

Geoffrey Flavell

1896. **Studies of Liver Function Tests. I. A Combined Intravenous Bromsulfalein–Hippuric Acid–Galactose Test**
L. ZIEVE, E. HILL, and S. NESBITT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 705–709, Nov., 1950. 5 refs.

The authors have compared the results of three liver function tests—the bromsulphalein, hippuric acid, and galactose tolerance tests—carried out separately and simultaneously in patients with liver disease and in

normal subjects. Each determination was made separately on successive days, and on the 4th day a combined test was performed. Bromsulphalein and galactose determinations were made on blood taken 45 minutes after injection, and hippuric acid determination in a 60-minute specimen of urine. The combined test was made by injecting intravenously a dilution of the standard doses of all three substances in 400 ml. of isotonic saline or glucose solution. There was no reaction, local or general, to the injection.

The combined test gave results closely similar to those of the three tests separately in both normal subjects and those with liver diseases (portal cirrhosis, infective hepatitis, passive congestion, and serum hepatitis).

B. G. Maegraith

1897. **Blood Test for Cancer**

M. M. BLACK. *Review of Gastroenterology* [*Rev. Gastroent.*] **17**, 481–487, June, 1950. 13 refs.

The author describes 2 tests based on the detection of changes in plasma reducing power and heat sensitivity in cases of cancer, which, while not absolutely specific, are claimed to be of value as an aid in diagnosis and follow-up. The first test is performed as follows. To 1 ml. of plasma or serum in a Wasserman tube are added 0·2 ml. of 0·15% methylene blue in distilled water, specially standardized, and a drop of capryl alcohol to prevent frothing. After mixing, the tube is immersed in a boiling water bath and the time taken for decolorization is noted. With serum from 1,000 normal subjects the distribution curve of results had a peak at about 8·0 minutes, and an upper limit of 10·0 minutes. With serum from cases of malignant disease the reducing time was increased up to a maximum of 20 minutes, and was over 11 minutes in 40 to 73% of cases of cancer of various sites. The author considers that this change is due to a change in location of an SH group in a protein component of the plasma, possibly albumin. To test this theory various substances were therefore added, in equimolar concentration, to 0·2 ml. of 0·13% methylene blue solution and the tubes immersed in a boiling water bath until decolorized. The tube containing methionine (no free SH bond) failed to change colour in 90 minutes, whereas decolorization of cystein hydrochloride (terminal SH bond) took 6 minutes and of glutathione (internal SH bond) took 15 minutes.

The second test depends on the fact that while the serum albumin level tends to fall in malignant disease, the serum fibrinogen level tends to rise and the serum thus becomes more heat sensitive. To perform the test 1·0 ml. of plasma is put in a Klett colorimeter tube and diluted to the 5·0-ml. mark. The colorimeter reading is taken and the tube immersed in boiling water for exactly 10 seconds, cooled, and the reading taken again. The difference between the two readings is the " coagulation value " and varies with different colorimeters. It exceeded 80 on the author's colorimeter in only 1% of normal sera tested, whereas it was over 80 in more than 60% of samples from patients with cancer.

Malignant disease was diagnosed by means of these tests in 416 out of 468 confirmed cases, and the test values returned to normal 7 to 10 days after extirpation of the neoplasm. False positive results were given by serum from cases of tuberculosis, rheumatic fever, cirrhosis of the liver, and pregnancy, but when these conditions were excluded 91% accuracy was obtained in 558 normal cases of non-neoplastic disease, and 92% in 116 cases of benign neoplasm.

Peter Harvey

BLOOD

1898. **The Dilution of Plasma in Estimating Prothrombin Activity.** [In English]

S. SHAPIRO and M. WEINER. *Acta Haematologica* [*Acta haematol., Basel*] **3**, 241–247, May, 1950. 3 figs., 6 refs.

Various methods of estimating prothrombin activity are considered and the conclusions reached are that determination of the prothrombin time of whole plasma and of 12·5% saline-diluted plasma, with rabbit lung thromboplastin, is the method best suited for routine work. The result is recorded in seconds.

A. Piney

1899. **Serum Prothrombin Time, a Composite Effect. An Analysis of the Factors Involved**

M. STEFANINI and W. H. CROSNY. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 1026–1036, Nov., 1950. 33 refs.

Quick's one-stage prothrombin consumption test (Quick, Shanberge, and Stefanini, *J. Lab. clin. Med.*, 1949, **34**, 761) determines the prothrombin content of serum and is valuable for the diagnosis of haemophilia and thrombocytopenic purpura. This paper is a study of the influence different variables exert on this procedure.

There are at least five coagulation factors involved: (1) the concentration of unconverted prothrombin in the serum; (2) the thrombin content of the serum, that is, that proportion of thrombin which has not been absorbed by fibrin or neutralized by the natural antithrombin; (3) the " accelerator effect " of the serum; (4) the labile factor " V ", plasma Ac-globulin not activated during coagulation; (5) (if coagulation has been completed more than 2 hours before the serum is tested) activation of a postulated prothrombin precursor. Of these five factors, three can be disregarded: the thrombin can be neutralized by incubation of the serum in the presence of citrate for 15 minutes, the concentration of labile factor can be ignored as it is added in excess, and the prothrombin precursor will not be activated provided not more than 2 hours are allowed to pass between coagulation of the plasma and the testing of the serum. The test is therefore mainly influenced by the concentration of residual prothrombin and the accelerator effect of the serum. Thus the test reflects not only prothrombin concentration, but also the velocity of the conversion of prothrombin into thrombin; it is a measurement of serum prothrombin activity rather than of concentration. However, in normal serum with full consumption of prothrombin no accelerator effect, however powerful, can compensate for this depletion; and since in abnormal serum in which consumption of prothrombin is defective the accelerator effect is also weak, from the

practical point of view Quick's test remains a measure of prothrombin concentration. *H. Lehmann*

1900. **Clot Retraction. Its Physiological and Clinical Significance**
A. J. QUICK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 538–546, Nov., 1950. 5 figs., 35 refs.

Washed platelets were suspended in a solution of fibrinogen and aliquots of 2 ml. placed in a series of test-tubes to which increasing amounts of thrombin were added. It was found that when the amount of thrombin added is very small, complete coagulation results but no clot retraction occurs. When the quantity of thrombin is increased, clot retraction occurs to a degree which is proportional to the amount of thrombin added. Further examples are given of the influence of thrombin on clot retraction. Other factors influencing clot retraction are the surface of the container, the haematocrit reading, and the presence of intact and discrete platelets. The author discusses these factors in relation to haemostasis and venous thrombosis. *A. Brown*

1901. **The Study of Capillary Permeability in Normal Subjects.** (Étude de la perméabilité capillaire chez le sujet normal)
R. CACHERA and F. DARNIS. *Annales de Médecine* [*Ann. Méd.*] **51**, 509–542, 1950. 4 figs., 32 refs.

Landis's test of capillary permeability, whereby the water and protein loss from the capillaries of the forearm during a period of venous stasis may be measured, was carried out on 24 normal subjects and the results compared with those obtained from the study of the rate of disappearance of Chicago blue 6B from the freely circulating plasma and the increase in its concentration during venous occlusion, which should also be related to capillary permeability. The following mean values were obtained in Landis's test: water loss 18·7 ml. per 100 ml. of initial blood, protein loss 0·22 g. per 100 ml. blood, protein content of the filtrate 1·1 g. per 100 mg. It was found that the rate of disappearance of the dye varied from subject to subject and was affected by numerous factors other than capillary permeability. Moreover, the concentration of Chicago blue during venous stasis did not always increase parallel with that of protein in the serum as determined in Landis's test, and its determination cannot therefore be substituted for the determination of protein concentration. *A. Schweitzer*

1902 (*a*). **The Electrical Conductivity of Blood. I. Relationship to Erythrocyte Concentration**
F. G. HIRSCH, E. C. TEXTER, L. A. WOOD, W. C. BALLARD, F. E. HORAN, and I. S. WRIGHT. *Blood* [*Blood*] **5**, 1017–1035, Nov., 1950. 8 figs., bibliography.

It has long been known that the electrical resistance of blood varies with the concentration of erythrocytes as well as its electrolyte content and other factors such as clotting, sedimentation, flow effects, and laking and haemolysis. In this paper from Cornell University Medical College, New York, further investigations into the characteristics of the electrical conductivity of normal blood are described. While it is generally agreed that estimation of blood conductivity may be used to measure packed erythrocyte volume, the authors have now shown that an exact correlation exists between the erythrocyte count and the electrical conductivity of normal blood. The apparatus used is fully described, with diagrams.

To determine the relative accuracy of visual and electrical counts experiments were carried out with suspensions of precisely known weights of packed erythrocytes in measured volumes of plasma; it was concluded that the conductivity method was the more accurate. To minimize errors in visual enumeration the counting chamber was photographed, but this did not improve the accuracy. The ratio of whole-blood conductance (K) to plasma conductance (K_o) was plotted against erythrocyte count for 33 specimens of normal blood, and the following equation derived from it relating the erythrocyte count per c.mm. (g) with conductivity: $g=C\times\frac{K_o-K}{K_o+K}$ where C is a constant whose value, calculated from estimations on 33 normal subjects, is 10·8 and X is a form factor, the value of which depends on the axial ratios of the cells assuming them to be spheroids, and for normal blood is 1·393.
T. M. Pollock

1902 (*b*). **The Electrical Conductivity of Blood. II. Relation to Red Cell Count**
E. C. TEXTER, F. G. HIRSCH, F. E. HORAN, L. A. WOOD, W. C. BALLARD, and I. S. WRIGHT. *Blood* [*Blood*] **5**, 1036–1048, Nov., 1950. 5 figs., 8 refs.

In this second paper (see Abstract 1902 (*a*)), studies of the relation between conductivity and erythrocyte concentration of the blood in various chemical states are described, and the possibility of using the measurement of conductivity as a reliable means of determining the erythrocyte count discussed. The equation given above, which was found to be accurate for normal blood, did not give such precise results with pathological blood samples for which a second equation, $g=C_1\frac{K_o-K}{K_o+K}$ (equivalent to the first with X assumed to be unity), was used. The arithmetical mean value of C_1 for 157 specimens was found to be 10·49. The results of erythrocyte counts by the visual and conductivity methods in a large variety of pathological conditions are presented, the standard deviation of 0·45 million between the two being ascribed to error in the visual method. With the most experienced technicians counting a large number of squares an error of 0·8 million per c.mm. must be allowed for in visual erythrocyte counts, whereas by the electrical method the corresponding figure is 0·24 million, a number of well-known sources of error in the visual count being eliminated. The authors admit, however, that the value given for C, and the equation itself, may require some modification. A nomograph is presented enabling the erythrocyte count to be read directly from the values obtained for the specific conductance of plasma and whole blood.
T. M. Pollock

Microbiology

1903. **Immunological Reactions of the Coxsackie Viruses. I. The Neutralization Test: Technic and Application**
J. L. MELNICK and N. LEDINKO. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 463–482, Nov., 1950. 2 figs., 23 refs.

After various preliminary tests which indicated that the Coxsackie group of viruses were unaffected by the range of temperatures usually encountered in carrying out virus neutralization tests, that complement was unnecessary, that the same end points were obtained with subcutaneous and intraperitoneal inoculation, and that neutralized mixtures of immune sera and virus could be reactivated by dilution, the authors showed that neutralizing antibodies appear on the 5th day of human infection, rapidly increase to a titre of 1 in 1,250 which is maintained for 1 to 3 months, and then diminish, but may still be present at a titre of 1 in 50 to 250 after 2 years. Examination of 200 children in North Carolina showed that antibodies for the High Point strain were present in 14% at the age of one year, and were at the adult level in 80% of those aged 7 years.

R. Hare

1904. **Immunological Reactions of the Coxsackie Viruses. II. The Complement Fixation Test**
L. M. KRAFT and J. L. MELNICK. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 483–497, Nov., 1950. 2 figs., 13 refs.

Antigens were made by homogenizing in saline the torsos of infected mice killed on the first day of paralysis. They were centrifuged lightly and then at 18,000 r.p.m. for 30 minutes. These crude antigens were then further purified by the addition of 5 mg. dry protamine sulphate, per 1 ml. and removal of the precipitate which formed by centrifugation. The crude antigen could also be concentrated and purified by centrifugation at 39,460 r.p.m. with re-suspension of the sediment in one-twentieth of the original volume of cold veronal saline, and removal of non-specific materials by protamine sulphate.

With hyperimmune sera prepared in mice or monkeys and the Kolmer or Fulton and Dumbell (*J. gen. Microbiol.*, 1949, **3**, 97) methods of complement fixation, 7 strains of Coxsackie virus (High Point, Connecticut-5, Texas-1, Ohio-1, Easton-2, Tompkins, Fleetwood, and Olson) were found to belong to six immunologically distinct types.

R. Hare

1905. **Immunological Reactions of the Coxsackie Viruses. III. Cross-protection Tests in Infant Mice Born of Vaccinated Mothers. Transfer of Immunity through the Milk**
J. L. MELNICK, N. A. CLARKE, and L. M. KRAFT. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 499–505, Nov., 1950. 9 refs.

Immunity to the Coxsackie group of viruses can be transferred to newborn mice by means of the colostrum or milk of vaccinated mothers. Whether or not placental transmission of immunity also occurs was not determined. Because the immunity transferred in this way is type specific it is possible to employ newborn mice from vaccinated mothers for determination of type, provided the challenging dose of virus does not exceed 100 ID 50.

R. Hare

1906. **Q Fever in Great Britain. The Causative Agent**
M. G. P. STOKER. *Lancet* [*Lancet*] **2**, 616–620, Nov. 25, 1950. 1 fig., 12 refs.

Two strains of *Rickettsia burnetii* isolated in Great Britain, one from a patient with Q fever, the other from milk, were compared in the laboratory with a standard Italian strain. The British strains were similar in shape, size, and pathogenicity for the guinea-pig. The milk strain was more readily adapted to growth in the yolk-sac of fertile hens' eggs, and appeared more pathogenic for guinea-pigs than the human strain. There was complete cross-protection with all three strains in guinea-pigs. Antisera against the British strains reacted with antigens from the Italian strain, but antigens from the British strains would not react until they were prepared from strains which had become adapted to the egg. A change in antigenic structure during egg adaptation is suggested as the explanation.

J. E. M. Whitehead

1907. **Pure Culture of *Rickettsia prowazeki* on Artificial Medium. The Phenomenon of Diseased Bacteria.** (Ein neuer Weg in der Fleckfieberforschung. Der Erreger auf künstlichen Nährböden reingezürchtet. Das Phänomen der kranken Bacterien)
W. SPÄT. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. 1 Abt., Originale* [*Zbl. Bakt.* (1 *Abt., Orig.*)] **156**, 171–179, Nov. 25, 1950. 8 refs.

1908. **Sensitivity of Diphtheria Bacilli and Related Organisms to Nine Antibiotics**
G. G. JACKSON, C. SHIH-MAN, E. H. PLACE, and M. FINLAND. *Journal of Pediatrics* [*J. Pediat.*] **37**, 718–726, Nov., 1950. 2 figs., 9 refs.

In this paper from Boston, the authors report the results of sensitivity tests *in vitro* on virulent strains of *Corynebacterium diphtheriae* and related organisms performed simultaneously with 9 different antibiotics. The strains used were classified as mitis, gravis, intermedius, xerose (producing acid from dextrose and sucrose but not from starch), and diphtheroids. The antibiotics used were: (1) bacitracin, 40 units per mg., (2) crystalline penicillin G., 1,595 units per mg., (3) terramycin hydrochloride, (4) chloramphenicol, (5) neomycin sulphate, 173 units per mg., (6) crystalline aureomycin hydrochloride, (7) streptomycin, (8) polymyxin B (aerosporin), and (9) polymyxin (polymyxin D, or "B.71"). They found that on a weight basis the different antibiotics can

be arranged in order of potency according to the list set out above. This is the only group of organisms pathogenic to man against which bacitracin is more active than penicillin. The range of activity shows that bacitracin in a concentration of 0·2 to 0·4 μg. per ml. inhibits 89% of strains, while penicillin in a concentration of 0·2 to 0·5 μg. per ml. inhibits 86%. At the bottom of the list, it was found that profuse growth occurred in concentrations of 200 μg. per ml. of polymyxin B and polymyxin D. Comparison of the concentrations which produced partial and complete inhibition gave interesting results. The antibiotics tested fall into two groups. One, which contains penicillin, bacitracin, polymyxin B, and chloramphenicol, will completely inhibit growth in a concentration 2 to 4 times greater than that which is necessary to produce partial inhibition. In the other group of antibiotics an 8- to 16-fold increase of concentration would be necessary. Discussing practical applications the authors suggest that the concentration of bacitracin required is too toxic except for local application. The plasma concentration of penicillin, terramycin, and chloramphenicol required could be maintained with safety, however, and these antibiotics may have therapeutic potentialities in diphtheria.

William Hughes

1909. **The Mutative Action of Penicillin I.N.Z. on Certain Pathogenic Gram-negative Bacilli.** (L'action mutative de la pénicilline I.N.Z. sur certains bacilles pathogènes Gram-négatifs)
K. S. Sotirova. *Revue d'Immunologie et de Thérapie Antimicrobienne* [*Rev. Immunol.*] **14**, 322–331, 1950. 2 refs.

Filtrates of *Penicillium crustosum* added to cultures of *Salmonella typhi*, *S. paratyphi* A and B, *Shigella dysenteriae*, and *Sh. flexneri*, especially cultures in potato-extract glucose-broth medium, are capable of stimulating the development of variants showing forms of metabolic activity which are absent in the strains from which they were derived, and antigenically different from the parent strain. The variants so produced are stable. The "mutagenic" activity of the filtrates bears no relation to their penicillin content. *C. L. Oakley*

1910. **The Effect of Substances from Lichens on Tubercle Bacilli and Some Other Micro-organisms.** (Die Wirkung von Flechtenstoffen auf Tuberkelbacterien und auf einige andere Mikroorganismen)
A. Stoll, A. Brack, and J. Renz. *Schweizerische Zeitschrift für Allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path.*] **13**, 729–751, 1950. 1 fig., 33 refs.

1911. **The Influence of "Tween-80"-albumin on the Bacteriostatic Effect of Substances from Lichens on Tubercle Bacilli.** (Einfluss von Tween 80-Albumin (Dubos–Nährmedium) auf die wachstumshemmende Wirkung von Flechtenstoffen gegenüber Tuberkelbakterien)
A. Stoll, A. Brack, and J. Renz. *Schweizerische Zeitschrift für Allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path.*] **13**, 752–755, 1950. 13 refs.

1912. **Discussion on Clostridial Toxins in Relation to Type-specificity for Different Species of Host**
C. L. Oakley, H. E. Ross, G. Payling Wright, M. G. Macfarlane, W. S. Gordon, and W. E. van Heyningen. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 883–892, Nov., 1950. 48 refs.

1913. **Studies on the Life Cycles of Spirochetes. II. The Development of a New Stain**
E. D. DeLamater, M. Haanes, and R. H. Wiggall. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 515–518, Nov., 1950. 7 figs., 7 refs.

A new modification of Fontana's stain for *Treponema pallidum* is described. After preliminary treatment with Ruge's fixative solution followed by Fontana's mordant fluid, the smears are placed in a solution of carbol methyl violet (saturated solution of methyl violet, 1 part, and 5% aqueous carbolic acid, 10 parts) for a minimum of 2 minutes. The smears are then dipped in distilled water, drained on filter paper, dipped once in acetone, dried between filter papers, and passed through a gentle flame. Finally they are placed in xylene and mounted in balsam or "permount".

The treponemes are stained deep violet-purple and when viewed through gamma blue-green and amber glass filters, or "Kodak" filters B 68 and G 15 or E 22, the contrast is sufficient for photography. Excellent photomicrographs of *T. pallidum* and of mouth spirochaetes are reproduced, which show the capabilities of the method. *V. E. Lloyd*

1914. **Immobilization of *Treponema pallidum in vitro* by a Specific Antibody Produced in Syphilis and Complement**
J. Archambault. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 483–485, Nov., 1950. 4 refs.

Employing the technique of Nelson (*J. exp. Med.*, 1949, **89**, 369) the author demonstrated the presence of immobilizing antibody (I.A.) against *Treponema pallidum* in the serum of syphilitic patients. In order to obtain a supply of *T. pallidum*, rabbits were given 2 injections of 0·5 ml. of a suspension of these organisms into the testicles; 24 hours after orchitis had developed the animals were killed and each testicle was cut into 10 slices and washed with chilled 0·85% saline; the slices were then placed in 40 ml. of Nelson's medium in an atmosphere of 5% carbon dioxide in nitrogen at 35° C. for 2 hours. The number of spirochaetes in the medium was adjusted by dilution to 10 million per ml., and the suspension separated from the testicular debris by centrifugation at 1,000 r.p.m. for 10 minutes.

In carrying out the test, 0·05 ml. of the serum to be examined (inactivated) is mixed with 0·05 ml. of guinea-pig complement and 0·4 ml. of the suspension of spirochaetes; as a control the same mixture is prepared, but the complement is previously inactivated. The tubes are incubated for 18 hours at 25° C. in a Brewer's anaerobic jar in an atmosphere of 5% carbon dioxide in nitrogen. A positive reaction is indicated if a large proportion of the organisms (at least 70%) are immobilized, and a negative reaction if most of the organisms

are still active. The difference between the two tubes should be at least 50% for a positive result, and a negative reaction should be confirmed by proving the presence of active complement by the addition of sensitized cells. The immobilized spirochaetes can be shown to have lost their virulence by injecting them into rabbits.

The immobilizing antibody differs from reagin; the latter is removed from syphilitic serum by absorption with Kahn or similar antigen, but the I.A. is not; also the serum reagin level can be shown to decrease under antisyphilitic treatment, though the I.A. does not. Thus it would appear that I.A. is closely associated with immunity.

The serum of most patients with syphilis beyond the primary stage gives a positive immobilization reaction, whereas that of normal persons and those suffering from diseases other than syphilis invariably gives negative reactions; this test may therefore be a valuable means of distinguishing true from biologically false positive reactions in the serum tests for syphilis. As yet the test cannot be used for the routine diagnosis of syphilis owing to technical difficulties, but if and when virulent *T. pallidum* can be cultured successfully it will have a wide clinical application. *T. E. Osmond*

1915. **The Cellular and Immunological Reactions in Rabbits Infected with *Histoplasma capsulatum***
G. J. Scheff and I. M. Pfeifer-Scheff. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 374–389, Oct., 1950. 3 figs., 29 refs.

The literature concerning *Histoplasma capsulatum* is briefly reviewed and a report given on observations made on rabbits infected by various routes with several strains of *H. capsulatum* with reference to their cellular and immunological reactions at different intervals.

Three groups of rabbits were inoculated with the mycelial form of *H. capsulatam*: one group intravenously and intraperitoneally, the second intraperitoneally, and the third intravenously. A fourth group were inoculated intravenously and intraperitoneally with the yeast-cell form. A fifth group were inoculated subcutaneously with the mycelial form. In the rabbits inoculated with the mycelial form of *H. capsulatum* a generalized chronic infection occurred, while in those inoculated with the yeast-cell form a more severe acute illness was induced. In both types of infection there was a transitory rise in the total leucocyte count, with an absolute rise in monocyte and a relative, but not absolute, depression of lymphocyte count. Some of the animals inoculated with the yeast-cell form died; before death the monocyte count was seen to be rising and *H. capsulatum* was recovered on blood culture. Histological examination of tissues from these animals revealed a granulomatous reaction in various organs, and the mononuclear macrophages contained intracellular yeast forms of *H. capsulatum*.

In rabbits inoculated intraperitoneally, lesions macroscopically similar to milk-spots appeared on the omentum. These increased in number and size for 2 to 3 weeks and were found microscopically to consist of monocytes, clasmatocytes, epithelioid cells, and Langhans-type giant cells. At 3 to 4 weeks the lesions were found to be diminishing, and at the end of 6 weeks after inoculation had completely disappeared. In the animals inoculated subcutaneously with the mycelial form the affected area became, within 48 hours, an inflammatory focus with a necrotic centre, around which was an area much infiltrated with neutrophils and monocytes. Yeast cells were demonstrated at the border of the necrotic centre and were recovered by culture.

Skin sensitivity to histoplasmin, of a lasting duration, occurred in all animals with a generalized infection. It developed 10 to 78 days after inoculation. The complement-fixation test became positive after 3 weeks and remained positive in the surviving animals for 206 days, at which time the experiment was concluded.
A. G. S. Heathcote

1916. **The Antibiotic Action of Protamine and Histone against Dermatophytes and Yeasts *in vitro*.** (Acción antibiótica *in vitro* de la protamina e histona frente a dermatofitos y candidas)
M. Pereiro Miguens. *Actas Dermo-Sifiliográficas* [*Actas dermosifiliogr., Madr.*] **42**, 12–16, Oct., 1950. 3 figs., 6 refs.

IMMUNITY

1917 (*a*). **Studies on Commercial Typhus Vaccines. I. The Antigenic Constituents of Commercial Epidemic Typhus Vaccine**
L. A. Chambers and J. R. Clawson. *Journal of Immunology* [*J. Immunol.*] **65**, 451–457, Nov., 1950. 14 refs.

An investigation has been made of the antigens present in 24 batches of commercial typhus vaccine prepared from infected yolk sacs. The rickettsiae were removed by centrifugation and the sediment and supernatant fluid were examined for the presence of complement-fixing antigens. These were still present in considerable amount in the rickettsia-free supernatant fluid; this soluble antigen was non-specific, whereas the separated rickettsiae were epidemic specific. From the yield of rickettsiae obtained it was calculated that one gramme of infected yolk sac contained an average of 0·43 mg. of rickettsiae. The yield was considered to be too low for the production of a concentrated and purified vaccine to be feasible, but fractionation of commercial vaccine might be of value for the production of reagent antigens of high titre. *D. J. Bauer*

1917 (*b*). **Studies on Commercial Typhus Vaccines. II. The Antigenic Fractions of Disrupted Epidemic Typhus Rickettsiae**
L. A. Chambers, S. S. Cohen, and J. R. Clawson. *Journal of Immunology* [*J. Immunol.*] **65**, 459–463, Nov., 1950. 9 refs.

Rickettsial concentrates obtained by the centrifugation of commercial typhus vaccine were disrupted by ultrasonic vibration and separated into three fractions by centrifugation, the sediment from low-speed centrifugation, and the supernatant fluid and sediment from

subsequent high-speed centrifugation of the supernatant fluid from the low-speed stage. Determinations were made of the nitrogen content of the three fractions. The low-speed sediment contained about half the nitrogen and complement-fixing activity of the original concentrate: the antigen was non-specific, and tryptic digestion of the fraction produced a rise in complement-fixing titre. The high-speed sediment contained one-third of the original nitrogen and two-thirds of the complement-fixing antigen, which was comparatively specific; tryptic digestion of the fraction caused a rise in complement-fixing activity to murine type antibody. The supernatant fluid from high-speed centrifugation contained only small amounts of nitrogen and complement-fixing antigen. The electrophoretic mobility of the three fractions was also investigated. *D. J. Bauer*

1917 (*c*). **Studies on Commercial Typhus Vaccines. III. The Concentration and Isolation of the Rickettsia-specific Soluble Antigen of Commercial Typhus Vaccine**
S. S. COHEN, L. A. CHAMBERS, and J. R. CLAWSON. *Journal of Immunology* [*J. Immunol.*] **65**, 465–473, Nov., 1950. 8 refs.

The soluble antigen of commercial typhus vaccine was sedimented by centrifugation in a field of 90,000 " g " for 40 minutes; a yield of up to 75% of the total complement-fixing activity was obtained. The material was examined in the analytical ultracentrifuge and electrophoresis apparatus; two components were present, one of which occurred to the extent of only 10%. The general properties of the antigen agreed with those of the soluble antigen isolated by Cohen and Chargaff (*J. biol. Chem.*, 1944, **154**, 691). It contained 9·58% nitrogen, 0·99% phosphorus, 5·05% carbohydrate, and 5·01% reducing sugar; it represented about 5% of the total nitrogen of the original vaccine. The remainder was made up mostly of non-specific protein. Attempts to isolate the antigen from crude vaccine by precipitation with ethyl alcohol or magnesium sulphate were not successful; the antigen could be precipitated, however, by adding antiserum to murine rickettsiae or *Proteus* OX-19, and the precipitated antigen still retained the power to produce epidemic antibody in rabbits. The antigen could be precipitated from crude vaccine by adding phenylhydrazine-*p*-sulphonic acid and acidifying to *p*H 2; a precipitate was formed which on separation and redissolving at *p*H 7 was found to contain over 90% of the original complement-fixing activity. The nitrogen content could be reduced to nearly one-third by dialysis without loss of activity. Antigen prepared by this method was still active after freeze-drying. The soluble antigen was also precipitated by sodium sulphite at a concentration of 20%. *D. J. Bauer*

1917 (*d*). **Studies on Commercial Typhus Vaccines. IV. The Chemical Composition of the Antigens of Commercial Typhus Vaccine**
S. S. COHEN. *Journal of Immunology* [*J. Immunol.*] **65**, 475–483, Nov., 1950. 33 refs.

Rickettsial antigen prepared by the high-speed centrifugation of suspensions of sonically disrupted organisms was not agglutinated by an antiserum to the cytoplasmic particles of yolk-sac endothelium; the rickettsial antigen was thus relatively free from antigens derived from the host. The three fractions obtained from disrupted rickettsiae by centrifugation (described in the second paper of the series) were analysed for their content of nitrogen, phosphorus, carbohydrate, and amino-acids both before and after digestion with proteolytic enzymes, and the results are given in tables. Digestion caused a loss of up to 80% of the tryptophan content without loss of antigenic activity. The lipid content was also determined and amounted to as much as 37·3%. The presence of desoxyribose nucleic acid in amounts up to 2·5% was demonstrated by colour reactions. This nucleic acid was isolated from the high-speed supernatant fraction in the form of the sodium salt; the solution had a low viscosity, and the nucleic acid had evidently been depolymerized during the process of sonic disruption. Ribose nucleic acid was apparently absent. Some abnormalities were observed in the colour reactions for carbohydrates, which suggested that the carbohydrates in rickettsiae are organized in some unusual pattern.
D. J. Bauer

1918. **Effects of Penicillin and Streptomycin on Vaccine Lymph**
V. N. KRISHNAMURTHY. *British Medical Journal* [*Brit. med. J.*] **2**, 1035–1037, Nov. 4, 1950. 11 refs.

Certain facts which had become evident during laboratory investigation and clinical application of penicillin and streptomycin could be demonstrated also in this study of antibiotic activity in the purification of vaccine lymph. If penicillin is added to glycerinated vaccine lymph at 4° C. and removed after one week by washing, colony counts of 238 millions per ml. are observed. If, however, the penicillin–lymph mixture is incubated at 37° C. a considerable reduction of the colony count is obtained. This is a clear demonstration of the known fact that penicillin acts only on growing micro-organisms. The effect of streptomycin on the number of staphylococci in lymph, when kept in cold storage, is very marked and the reduction in numbers is proportionate to the concentration of streptomycin. When both antibiotics are combined in low concentration a reduction occurs comparable to that produced by 10 times the concentration of streptomycin. The same phenomenon occurs if the antibiotics are incubated with lymph at 37° C. for 24 hours.

A reduction of the bacterial count to 200 organisms per ml. of vaccine can be obtained also if a combination of penicillin and streptomycin is applied to the vaccinated area of the calf twice daily for 5 days. The concentrations of the antibiotics per ml. used can be varied from 100 units penicillin and 1,000 μg. streptomycin to 100 units penicillin and 10,000 μg. streptomycin without reducing the bacterial count below 200 organisms per ml. In this, as in the previous experiments, *Bacillus subtilis* spores were not inhibited. No loss of potency of the lymph treated with antibiotics could be detected.
K. Zinnemann

Paediatrics

1919. **The Relation of Birth Weight to Physical Growth. A Statistical Study**
R. S. ILLINGWORTH, C. C. HARVEY, and G. H. JOWETT. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 390–388, Dec., 1950. 6 figs., 7 refs.

The authors have extended their previous work (*Lancet*, 1949, **2**, 598) on the relation of birth weight to subsequent weight and height by investigating other standard body dimensions in groups of children of different birth weights. The object was to ascertain whether such measurements would account for the subsequent differences in weight found in children of different birth weights. A total of 238 children between the ages of 5 to 8 years were studied and were divided into three groups according to their birth weights: 5½ lb. (2·5 kg.) or less; 7 lb. 2 oz. to 7 lb. 6 oz. (3·2 to 3·35 kg.); 8½ lb. (3·85 kg.) or more. The standard body dimensions examined were weight, pelvic and calf girth, chest circumference, and standing and sitting height. The methods used to obtain these measurements are described. They found that all the measurements were smaller in those of low birth weight than in those of large birth weight and that the measurements of children of average birth weight fell between the two. These findings were found to be statistically significant (there is an appendix to the paper in which the statistical methods used are described). Emphasis is placed on the importance and possible long-term effects of controllable factors that influence birth weight, such as premature induction of labour, and the prevention of prematurity by the improvement of the nutritional and social circumstances of the mother. *David Morris*

1920. **"Tween 20" and Fecal Fat in Premature Infants. A Preliminary Study**
A. L. JOHNSON, R. B. SCOTT, and L. H. NEWMAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 545–550, Oct., 1950. 10 refs.

1921. **Feeding of Premature Infants. Use of a Simple Formula**
S. M. ABELSON. *Journal of Pediatrics* [*J. Pediat.*] **37**, 711–717, Nov., 1950. 18 refs.

The object of this paper is to confirm the work of Adams (*J. Pediat.*, 1948, **33**, 23), who found that feeding premature babies with equal parts of evaporated milk and water without added carbohydrates gave better results than more orthodox methods. A series of 311 premature babies were placed under the following regime: no feeds were given for 36 to 72 hours, then glucose water every 3 hours for 12 hours. During the next 24 hours glucose water and half-strength evaporated milk were alternated, and finally the milk feeds were given alone. The amounts given were 8 ml. for an infant of 1,500 g. (3 lb. 5 oz.), 4 ml. for a child of 1,100 to 1,200 g., and 15 ml. for an 1,800-g. baby. All feeds were given by gavage for babies under 2,000 g. (4 lb. 6 oz.). Increases were made gradually until a daily intake of 150 to 200 ml. per kg. was reached, which usually occurred during the 2nd week. In addition water-soluble multivitamin preparations were given. On the day after starting oral feeding, oxygen and antibiotics were used freely, crude liver extract, 1 ml. intramuscularly, was administered twice weekly after the 5th day, and ferrous sulphate elixir was given from the age of 1 month. The mortality was 17%, whereas in the rest of the U.S.A. the death rate among premature infants is 27%. The stay in hospital was shorter and the gain in weight more rapid than under orthodox treatment. Although spontaneous acidosis, manifested by hyperpnoea and apathy, occurred in 8 infants, these all recovered on being given 10 to 15 grains (0·65 to 1·0 g.) of sodium bicarbonate daily and/or Ringer–lactate solution parenterally.

[These babies did remarkably well, but it is hardly justifiable to attribute it to the method of feeding alone when so many other therapeutic and preventative measures were adopted. It is a pity that a control group of babies were not put on the same regime but fed with expressed breast milk.] *J. Vernon Braithwaite*

1922. **Cephalohematoma in the Newborn**
M. D. INGRAM and W. M. HAMILTON. *Radiology* [*Radiology*] **55**, 503–507, Oct., 1950. 7 figs., 8 refs.

The authors present a statistical analysis of 126 cases of neonatal haematoma. The average incidence of this condition was 1·66% in a total of 7,563 deliveries, but the analysis shows that it was more frequent when forceps had been used. The average birth weight of the infants suffering from cephalhaematoma was significantly higher than that of normal infants. Four typical cases of calcifying cephalhaematoma in the newborn are described in detail, and the clinical features of cephalhaematoma are discussed. *A. Orley*

1923. **Nursery Infections**
K. CAMPBELL. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 138–142, Jan. 27, 1951. 1 fig., 5 refs.

It is inevitable for infections to occur in nurseries since so many people now have access to them and so many people actually handle the babies. Before an infection is sufficiently obvious to attract attention it must have been present for a certain time and it is this lag that constitutes the danger. The problem may be studied under four heads: the modes of introduction of infection, modes of transmission, general measures for preventing spread and introduction, and specific measures to prevent spread when infection has become established. The author discusses infection under these four headings and describes the regime required in a nursery and the various steps to be taken when infection has arisen. She stresses several points which are often ignored. For instance, charts, writing materials, and

stethoscopes are often in close contact with the infant and are rarely sterile. Nurses frequently imagine that infants' stools are sterile and do not wash their hands after contact. Workers in the laundry should report any illness since it may be a source of infection. She stresses the need for setting up a separate "clean" nursery directly infection becomes established in the main nursery. This must be staffed by a different set of nurses; although this is a strain on the organization, in the long run it is an economy in staff, since the infection will otherwise drag on endlessly. The author concludes with a description of the commoner types of infection encountered.

[A well-condensed review of the subject.]

J. G. Jamieson

1924. **Nutritional Edema.** [In English]
P. V. VÉGHELYI. *Annales Paediatrici* [*Ann. paediatr., Basel*] **175**, 349–377, Nov., 1950. Bibliography.

The effects are described of prolonged malnutrition on 109 infants, aged 3 to 18 months, fed mainly on dried vegetables and fats during the siege of Budapest in 1945. The principal clinical manifestation was a generalized oedema, preceded by steatorrhoea, loss of weight, pancreatic and hepatic dysfunction, hepatomegaly, hypoproteinaemia, and anaemia. In cases associated with various infections, however mild, the course of the disease was aggravated and the appearance of the oedema accelerated. No specific vitamin-deficiency syndromes were noted, nor did the condition permanently respond to any vitamin therapy. Parenteral administration of proteins was of no avail. Milk given in "sufficient quantities" had a dramatic therapeutic effect. The restoration of pancreatic enzyme reaction was succeeded by the disappearance of the oedema, decrease in the size of the liver, and restoration of the normal plasma protein level within 10 days. On the other hand, small quantities of milk (50 to 80 g. per day) or prolonged administration of aneurin produced a rapid deterioration of the condition. Relapse occurred in all cured infants within 3 weeks if the milk feeding was stopped, and the condition then proved irreversible, most patients dying within 10 to 14 days of the re-appearance of the oedema and 9 to 17 weeks after the milk feeds had ceased. The histological findings in the liver in cases without infection were of fatty degeneration, invariably at the periphery of the lobules but extending centrally in severe cases, especially in those fed on small amounts of milk with additional nicotinic acid. The pancreas showed a diffuse cloudy swelling and, in more advanced cases, an atrophy of the acinar cells and fibrosis. The islet cells remained unaffected. In cases associated with infection the changes seemed less extensive, but the fatty infiltration of the liver was more centrilobular. Re-examination within 2 to 3 years revealed no abnormality in the surviving children (39), apart from some retardation in growth (minus 9 months) compared with the Hungarian standard. The liver remained palpable for 2 to 4 months, but liver function tests became normal within 3 to 6 months. It seems obvious that the lack of certain constituents of the milk, most probably deficiency of the complete range of proteins, was the cause of the condition. Animal experiments and observation in man confirm that liver damage, due to cystine and methionine deficiency, may be caused by feeding on a diet consisting solely of carbohydrates.

The liver damage in kwashiorkor and in tropical fatty liver disease in Jamaican children is described and the author also discusses the hormonal inter-relationship between pancreas and liver experimentally proved in animals. The inhibition of the pancreatic enzyme activity in consequence of a deficient diet might have initiated the hepatic changes. Further investigations of the complex pathogenesis are proposed.

[The paper is full of interesting details. Some inconsistency in the reported facts may have been caused by wartime conditions.] *M. Dynski-Klein*

1925. **The Use of "Sangamin", a New Protein Hydrolysate, in Meeting the Increased Protein Requirements of Premature and Marasmic Infants.** (Die Deckung des erhöhten Eiweissbedarfs von Frühgeburten und dystrophischen Säuglingen mit Sangamin, einem neuen Eiweisshydrolysat)
H. PLÜCKTHUN and K. SCHREIER. *Kinderärztliche Praxis* [*Kinderärztl. Praxis*] **18**, 508–514, Nov.–Dec., 1950. 2 figs., 23 refs.

1926. **Congenital Deficiency of Abdominal Musculature with Associated Genitourinary Abnormalities: a Syndrome. Report of Nine Cases**
J. F. EAGLE and G. S. BARRETT. *Pediatrics* [*Pediatrics*] **6**, 721–736, Nov., 1950. 11 figs., 38 refs.

The authors emphasize the importance of urethral obstruction as a cause of the common finding of gross enlargement of the bladder, mega-ureter, and hydronephrosis. The condition is almost exclusively found in the male. Although in most cases the child succumbs during its first year to pneumonia and pyelonephritis, a few instances of survival have been recorded. The theories so far presented to account for the association of the defects of the abdominal musculature and of the genito-urinary tract are criticized, and therapeutic measures are described for the relief of urinary obstruction.

W. G. Wyllie

1927. **An Outbreak of Atypical Pneumonia in a Children's Home.** (Endemie atypischer Pneumonien in einem Säuglings- und Kinderheim)
H. KÖRVER. *Kinderärztliche Praxis* [*Kinderärztl. Praxis*] **18**, 493–501, Nov.–Dec., 1950. 11 refs.

An outbreak of an influenza-like infection which affected 80% of the inmates of a children's home during May, June, and July, 1949 is described. Frequently associated with pneumonia it resembled clinically the "primary atypical pneumonia" of adults. The probability that the condition was due to a virus infection was supported by the following facts: the disease was highly contagious; there was a marked discrepancy between the clinical and radiological findings; examination of the blood showed no leucocytosis, but the presence of plasma cells and large monocytes; and the cold-agglutinin titre

was raised and the Hirst test positive in several cases. Animal experiments had to be abandoned after several passages. *W. Mestitz*

1928. **The Incidence of Oxyuriasis in Infants.** (Zur Frage des Oxyurenbefalls bei Säuglingen)
E. NEUMANN and H. R. WIEDEMANN. *Kinderärztliche Praxis* [*Kinderärztl. Praxis*] **18**, 556–561, Nov.–Dec., 1950.

It is well known that infants in the first year of life hardly ever suffer from threadworm infestation. Whereas the incidence of oxyuriasis among German schoolchildren since the war has been variously estimated as between 87% and 97·2%, the authors found only 5 cases amongst 300 infants attending a welfare clinic (1·66%). This " immunity " is accounted for by the fact that the milk diet is poor in residue, the frequent, soft motions, the isolation of the baby, and the attention which is paid to his cleanliness. Moreover, auto-reinfection does not occur. *W. Mestitz*

1929. **Pulmonary Infiltration and Blood Eosinophilia in Children (Loeffler's Syndrome). A Review with Report of Eight Cases**
R. L. NEMIR, A. HEYMAN, J. D. GORVOY, and E. N. ERVIN. *Journal of Pediatrics* [*J. Pediat.*] **37**, 819–843, Dec., 1950. 5 figs., bibliography.

Eight patients with pulmonary infiltrations and eosinophilia are described. Five of the cases were mild and corresponded to the original description of Loeffler's syndrome. Three cases were chronic and the condition persisted for months. These cases corresponded to the broader and more recent concept of Loeffler's syndrome. Three cases were for a time mistakenly diagnosed as of miliary tuberculosis because of the nature of the *x*-ray shadows and a positive reaction to tuberculin skin test. The importance of differentiating Loeffler's syndrome in patients with positive tuberculin reaction is emphasized.

Disturbed liver function was found in the 3 chronic cases. In 7 instances the pulmonary *x*-ray shadow cleared before the eosinophile count in the peripheral blood returned to normal levels.

All the patients survived. In 7 patients intestinal parasitism was found. In the eighth patient bacterial allergy associated with infected sinuses is suggested as the cause of the Loeffler's syndrome.—[From the authors' summary.]

1930. **Streptomycin in the Treatment of Infantile Diarrhoea.** (La streptomicina nel trattamento delle enteriti del lattante)
R. BULGARELLI and P. TOLENTINO. *Policlinico Infantile* [*Policlin. infant.*] **16**, 608–624, Dec., 1948 [received 1950]. 47 refs.

Previous work on the absorption and fate of streptomycin in the intestine, together with consideration of the reported sensitivity of various intestinal pathogens to the antibiotic, led the authors to use streptomycin in the treatment of 46 cases of diarrhoea in infants ranging in age from 15 days to 17 months. Of the 13 infants (aged 1 to 10 months) treated by the intramuscular injection of 40 mg. per kg. body weight 5 failed to respond. Of 5 infants (aged 2 to 10 months) treated by the rectal administration of 50 to 80 mg. per kg. only 2 responded, and in these the infection was confined to the lower bowel.

The remaining 28 patients (together with 5 of those who had failed to respond) were given the drug by mouth in 4 doses of 25 mg. per kg. daily, with only one failure. Recovery took 3 to 6 days on average, though some patients required a total of 10 to 15 days' treatment. The condition was usually primary, due to *Bacterium coli*, *Proteus vulgaris*, or *P. morganii*, but some cases were secondary to otitis, bronchopneumonia, etc. Many of the infants showed toxic signs.

The authors conclude that oral streptomycin is the treatment of choice in all forms of gastro-enteritis, that rectal administration should be used as an adjunct when only the lower bowel is involved, and that the intramuscular route should be reserved for cases showing signs of septicaemia. Primary foci should receive appropriate treatment with penicillin or sulphonamides.

E. R. Cole

1931. **Recurrent Abdominal Pain in Childhood**
E. S. STUCKEY. *Medical Journal of Australia*]*Med. J. Aust.*] **2**, 827–832, Dec. 2, 1950. 6 figs.

A series of 100 children suffering from abdominal pain in whom little could be found on clinical examination were investigated, appendicectomy performed, and the results observed for 2 to 3 years. An analysis is presented of the symptomatology, clinical, operative, and pathological findings, and end results in this series. The abdominal pain was recurrent, usually central in position but sometimes in the right iliac fossa, and accompanied by nausea, pallor, and listlessness. Slight tenderness was usually present at McBurney's point or at the lateral border of one or other rectus muscle at the level of the umbilicus. Occasionally there was suprapubic tenderness. Repeated clinical examinations were made, the urine examined microscopically and cultured, a blood count made and, in some cases, barium-meal examination and excretion urography performed. The conditions which were considered in differential diagnosis included intestinal colic due to *Oxyuris* infestation, constipation, or unsuitable diet, mesenteric adenitis, Meckel's diverticulum, congenital bands, internal herniae, Crohn's disease, upper respiratory infection, undiscovered renal abnormalities, testicular and ovarian pain, migraine, and cyclic vomiting. The position and appearance of the appendix, the state of the mesenteric lymph nodes, and the presence of any abdominal abnormality were noted at the time of the operation.

The chief findings were as follows: (1) When a barium-meal examination suggested disease of the appendix, such was usually found at operation. (2) Meckel's diverticulum was present in 3 cases, but in none was there disease of the diverticulum. (3) The appendix was most commonly retrocaecal (lying among coils of ileum) or pelvic in position, which might account for the absence of marked physical signs. (4) The mesenteric nodes were normal in 31 cases and doubtful in 27, enlargement

was limited to the ileo-caecal group in 28 cases and generalized (often without obvious disease of the ileo-caecal group) in 7. (5) Ileo-caecal adenitis was often due to recurrent appendicitis. (6) Generalized mesenteric adenitis was thought to be due to infection from Peyer's patches, but there was no sharp dividing line between these cases and those due to appendicitis. Lymphoid hypertrophy of the appendix was found in some cases. (7) Appendicectomy relieved the symptoms in some cases of generalized mesenteric adenitis. There was no correlation between relief of symptoms by appendicectomy and the presence of ileo-caecal lymph-adenitis. (8) In some cases of *Oxyuris* infestation the appendix did not show any microscopic inflammatory changes, while in other cases eosinophilia occurred in the absence of *Oxyuris* infection. (9) There was no correlation between the microscopical appearances of acute or chronic inflammation and cure by appendicectomy. (10) Appendicectomy cured the condition in 60 children and relieved it in 17; improvement was uncertain in 14 cases and there were 9 failures.

Charles P. Nicholas

1932. **First Clinical and Radiological Studies on the Action of New Synthetic Spasmolytic Drugs in Habitual Vomiting in Infancy.** (Prime ricerche cliniche e radiologiche sull'azione di nuova spasmolitici di sintesi nel vomito abituale del lattante)
R. BULGARELLI. *Lattante* [*Lattante*] **21**, 454–470, July, 1950. 9 figs., 6 refs.

The author discusses previous work on two spasmolytic drugs, "lyspamin" (phenobarbitone and dinicotinamido-1 : 2-diphenylethane) and "profenil" (bis-γ-phenylpropylethylamine), neither of which has been used previously in infants.

Working at the Institute of Clinical Pediatrics of the University of Genoa, he first investigated the effect of these two drugs on 10 normal infants, 5 of whom had been breast-fed and 5 bottle-fed. Their ages varied from 15 days to 6 months. They were first examined radiologically every hour for 4 hours following the ingestion of a barium meal. The following day, immediately after an identical barium meal, 5 infants received ¼ tablet of lyspamin, 3 others ¼ ampoule of profenil intramuscularly, and 2 others ¼ tablet profenil by mouth. (One lyspamin tablet contains 0·275 g. nicotinamido-diphenylethane and 0·025 g. phenobarbitone. One profenil tablet contains 0·036 g. bis-γ-phenylpropylethylamine, and 1 ampoule contains 0·04 g.).

Radiologically in each case there was a slight decrease in gastric movement and intestinal peristalsis. The rate of emptying of the stomach was not noticeably affected by any of the drugs used, being complete in 3 to 4 hours. It was considered that the slowing of peristalsis was offset by the effect of the drugs on the tone of the pylorus.

The author then proceeded to investigate the effect of these drugs in 20 cases of "habitual vomiting of infants", selecting those that he considered due to spasm of the pylorus and rejecting those due to hypertrophic stenosis. Ages varied from 4 to 60 days except for one girl aged 10 years who was treated for pyloric spasm; 13 patients had been breast-fed, 3 artificially, and 3 had mixed diets. Three of the infants were premature. Fifteen patients took ¼ tablet of lyspamin 6-hourly and 5 received either ¼ tablet or ¼ ampoule of profenil 6-hourly, and the progress of the barium meal was followed radiologically and clinically in each case. A detailed history is given for each patient.

The clinical results were very satisfactory and the radiological study showed that in an average of 3 to 5 hours gastric movements and intestinal peristalsis became less violent, there being considerable improvement in the emptying of the stomach. Vomiting ceased completely 2 to 8 days after the commencement of treatment, which varied in duration from 8 to 40 days. No relapses occurred after cessation of treatment. Most patients had previously been treated without success with atropine, "eumydrin", adrenaline, or ephedrine. Drowsiness was marked in those cases treated with lyspamin, and the author suggests a reduction in the proportion of phenobarbitone.

E. R. Cole

1933. **Notes on Cerebellar Ataxia in Childhood**
R. A. SHANKS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 389–391, Dec., 1950. 13 refs.

During the 20 years 1929–49 there were admitted to the Royal Hospital for Sick Children, Glasgow, 39 cases of cerebellar ataxia. These were not secondary to such conditions as subtentorial tumour, but constituted a "well recognized group of cases in which cerebellar ataxia is the only ultimate diagnosis". They are conveniently divided into those of sudden and those of insidious onset. Although the numbers were small the cases in the former group were in a younger age group, they tended to occur in the late summer and winter, and in 27% there was an antecedent illness. The progress after discharge was traced only in 30 cases. In those of sudden onset there were 13 complete recoveries out of 17, whereas there was only one complete recovery out of 13 in those of insidious onset. The author considers that these represent two distinct syndromes, the latter being composed of cases of degenerative ataxia, probably of genetic origin. In the early stages the clinical picture was similar in both groups and neither the changes in the cerebrospinal fluid nor the temperature chart were of help in diagnosis.

David Morris

1934. **The Therapeutic Association of Penicillin and Synthetic Antihistamine Drugs in Glomerulonephritis in Infancy.** (Considerazioni sull'associazione terpaeutica penicillina antistaminici sintetici nelle glomerulonefriti dell'infanzia)
V. BAFFI. *Pediatria* [*Pediatria*] **58**, 198–208, March–April, 1950. 34 refs.

The author, working at the Institute of Clinical Paediatrics of the University of Naples, treated 5 cases of glomerulonephritis in infancy with penicillin combined with antihistamine drugs. The patients' ages ranged from 20 months to 10 years. In every case the dosage of penicillin was 20,000 units intramuscularly every 3 hours for 10 to 15 days, and of the antihistaminic 0·1 g.

5 or 6 times daily by mouth, In every case the antihistaminic was continued after the cessation of penicillin treatment for periods up to 25 days.

The results are described as " brilliant ". In 3 of the cases the general condition improved and the oedema disappeared within 10 days, the blood pressure and the blood urea level became normal in 8 days, and albuminuria and haematuria had improved in 7 to 8 days and had completely disappeared after 11 to 12 days. In the other 2 cases the general condition had improved and the oedema had disappeared in 10 days, the blood pressure was normal after 12 days, and the urine was normal in 20 days. The author declares that in these cases treatment with penicillin and antihistaminic together produced results far superior to those obtained by the separate employment of either of them.

[The author unfortunately does not mention the chemical constitution of the antihistaminic employed.]

E. R. Cole

1935. **Reiter's Syndrome in Childhood**

B. D. CORNER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 398–403, Dec., 1950. 2 figs., 24 refs.

1936. **Thyroid Cancer in Childhood and Adolescence. A Report on Twenty-eight Cases**

B. J. DUFFY and P. J. FITZGERALD. *Cancer* [*Cancer*] **3**, 1018–1032, Nov., 1950. 11 figs., 19 refs.

There has been argument as to the occurrence of thyroid carcinoma in childhood, the main contentions being that conditions reported as such were really large cysts or tumours of thyroglossal remnants, or that the condition is such a relatively slow-growing one that it hardly deserves the name. The latter is in reference to the papillary type.

The authors review 28 cases of thyroid cancer in patients aged from 4 to 18 years at the time of histological diagnosis. All patients had had lymph nodes or thyroid nodules present for months or years which were later found to contain carcinoma. The 28 cases constituted 6·5% of 430 thyroid cancers seen in a 16-year period at a cancer hospital with a special paediatric clinic. Fifteen of the specimens showed papillary, 8 alveolar and follicular, 4 solid, and 1 a Hürthle-celled carcinoma. There was the usual amount of mixed pathology among the specimens, and the classification was based on the most prevalent type.

Long survival was noted both in the papillary and in the follicular and alveolar types. However, only 3 of the 16 cases of the former showed pulmonary metastases, compared with 6 out of 9 cases of the latter. While unable to draw significant conclusions the authors think the prognosis is poorest in solid carcinoma.

Details are given of lymph-node and pulmonary involvement; no skeletal metastases were noted. In an attempt to assess aetiological factors it is pointed out that most cases occurred in the few years preceding and following puberty.

Assessment of the various methods of treatment is regarded as unreliable since the natural history of untreated carcinoma is unknown; patients with some histological types survive for many years without treatment. None the less, in view of the failure of deep therapy and conservative surgery in thyroid carcinoma of this age group an aggressive surgical attack on the thyroid and cervical lymph nodes is advocated, radio-iodine and *x*-ray therapy being reserved for other metastatic lesions, and for patients in whom surgery is contraindicated.

Some illustrative detailed case records are presented.

Charles Donald

1937. **The Treatment of a Genuine Case of Juvenile Polymyositis (Dermatomyositis) with Penicillin.** (Die Behandlung einer kindlichen genuinen Polymyositis (Dermatomyositis) mit Penicillin)

F. H. DOST. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **140**, 183–190, 1950. 16 refs.

Polymyositis is a rare disease, and especially rare in children. The subject of this report was a 12-year-old boy admitted severely ill with generalized muscular spasm and pain almost completely preventing movement, including that of speech and swallowing. There was also subcutaneous oedema, mainly of the face, forearms, legs, and abdomen, a generalized skin eruption of rosy and livid patches, somewhat indurated but not raised, pleural effusion, nephritis, and a severe bilateral central retinitis. The diagnosis lay between polymyositis and some form of sepsis. The latter was unlikely in view of the fact that the temperature rarely rose much above 38° C., and muscle biopsy finally confirmed the diagnosis of polymyositis, once more drawing attention to the similarity of this condition to periarteritis nodosa.

Penicillin treatment was started on the 8th day after admission and, in all, 3,040,000 units was given. Improvement began after 4 days and continued, with the interruption of a slight relapse, after penicillin had been stopped for lack of supply; 10 months after the beginning of the illness the child was well, except for a much reduced visual acuity; 11 months after that he was still well, and vision had improved a little.

The author suggests that penicillin treatment be kept in mind in these cases, though he cannot ascribe the cure in his case for certain to this drug. If penicillin should prove to be effective some light would be thrown on the aetiology of this disease, which might then be regarded as an allergic response to a penicillin-sensitive bacterial infection.

Marianna Clark

1938. **Studies of Acid Base Equilibrium in Premature Infants**

H. S. REARDON, B. D. GRAHAM, J. L. WILSON, M. L. BAUMANN, M. U. TSAO, and M. MURAYAMA. *Pediatrics* [*Pediatrics*] **6**, 753–771, Nov., 1950. 1 fig., 8 refs.

A study of the acid–base equilibrium of 64 premature infants is presented: 87% of the infants were considered to be healthy. The infants varied from 1 to 65 days in age, and between 1·1 and 2·3 kg. in weight. In the majority a slight degree of metabolic acidosis was found in samples of arterial blood, equally in those classified well as in those sick. No evidence was obtained of hyperpnoea to indicate an increase of alveolar ventilation.

W. G. Wyllie

Medicine: General

1939. **Prophylaxis of Motion Sickness. Evaluation of Some Drugs in Sea Sickness**
H. I. CHINN, W. K. NOELL, and P. K. SMITH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 810–822, Dec., 1950. 17 refs.

An experiment was carried out in a U.S. Army troopship to discover whether there was any correlation between the antihistamine activity of a drug and its tendency to prevent sea-sickness, and to compare the potency in this respect of a series of antihistamine and other drugs. On the outward trip from New York, 608 volunteers, 47% of whom were making their first sea voyage, were divided into 7 groups according to the drug given. The first capsule of the drug was given at 6 p.m. (3 hours after sailing), and subsequent capsules were taken at 6 a.m., 11 a.m., and 6 p.m., the next day. The soldiers were given questionaries to complete before sailing and again en route, and interviews took place when feasible. On the return trip to New York 342 subjects were studied, all of whom had obviously already experienced sea travel.

It was found that the prophylactic activity of a drug was not related to its antihistamine activity, but was probably related to its anticholinergic activity. The most effective drugs were found to be diphenhydramine (" benadryl ") and " dramamine ". Hyoscine, although very effective, produced more side-effects. The incidence of drowsiness among those receiving drugs was no higher than in the group receiving the placebo. It would appear that acclimitization to sea travel takes place quickly, so that it is difficult to judge the curative, as distinct from the prophylactic, value of the drugs.

Electroencephalography was carried out on many of the patients. The ordinary alpha rhythm predominated, but in marked sea-sickness there was a predominant slow-wave pattern in some of the cases.

Paul B. Woolley

1940. **Effect of Carbon Dioxide on Rate of Denitrogenation in Human Subjects.**
R. MARGARIA and J. SENDROV. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 295–308, Dec., 1950. 3 figs., 38 refs.

In experiments carried out at the U.S. National Naval Medical Centre, Bethesda, Maryland, 4 subjects were exposed to pressures of 78 ± 3 cm. Hg above atmospheric for 4 hours and, after decompression in 1 minute, the rate of nitrogen elimination was measured over a period of 60 to 120 minutes, starting 10 to 15 minutes after decompression, during the inhalation of a nitrogen-free gas mixture. Analysis of the rates of nitrogen excretion showed that they might be expressed as a function of time by the sum of two terms of the type $Y = 10^{a-bt}$, the values of the velocity constants (b) being 0·0096 (half-reaction time 31 minutes) and 0·0022 (half-reaction time 137 minutes). The rate of nitrogen elimination was not significantly increased on breathing 3% carbon dioxide in oxygen. However, a 5% carbon dioxide mixture caused an increase of 70% in the velocity constant of the fast reaction (half-reaction time 19 minutes) and tended to retard the slow component. Increase in pulmonary ventilation *per se* had no effect on nitrogen elimination over the time interval studied, as shown by the results with 3% carbon dioxide or when a respiratory dead space was introduced. It is suggested that the effect of 5% carbon dioxide was mainly due to increased blood flow through some areas (watery tissues, responsible for the fast component) and to a possible decrease in the blood flow through others (fatty tissues, responsible for the slow component). The volumes of nitrogen dissolved in the body when air was breathed at one atmosphere pressure were, in respect of the two components, 373 and 532 ml. The inhalation of 5% carbon dioxide during the first 30 minutes of de-nitrogenation caused a 20% increase in nitrogen elimination compared with that during the inhalation of pure oxygen. It is suggested that the inhalation of carbon dioxide–oxygen mixtures may be useful in the prophylaxis of decompression sickness.

D. H. Sproull

1941. **Immersion and Survival in Cold Water**
E. M. GLASER. *Nature* [*Nature, Lond.*] **166**, 1068, Dec. 23, 1950. 11 refs.

The author points out that while a survey of the results of experiments performed in baths (Molnar, *J. Amer. med. Ass.*, 1946, **131**, 1046) suggests that few men could live in water near freezing point for more than 30 minutes, and none for more than 1½ hours, shipwreck survivors are known to have lived after spending several hours in icy seas, while Critchley (*Shipwreck Survivors, a Medical Study*, London, 1943) has quoted the case of a man who survived after swimming for more than half a day in water at −1·5° C. The author reports the results of experiments which may explain this apparent contradiction. The subject swam for 30 seconds in sea water at 3° C. When he emerged his skin temperature was only slightly reduced, and rose to its original value within 10 minutes. Rectal temperature rose by 0·4° C. immediately after the swim, the mechanism probably involved having been discussed elsewhere (Glaser, *J. Physiol.*, 1949, **109**, 366). The calculated heat loss in the water was 10 to 12·5 calories per minute, which should have lowered the body temperature by about 0·14° to 0·18° C. per minute, so that a few minutes immersion in very cold water would not cool the body to a dangerous extent. Determinations of the heat production during swimming showed that this would more than balance that lost by conduction from the body surface. It is suggested, therefore, that men in danger of immersion in cold water should be

advised to swim or struggle as long as possible. In clinging to lifebelts or wreckage to save their strength they may die of cold. *R. A. Gregory*

1942. **Effects of Pituitary Adrenocorticotropic Hormone (ACTH) on the Hypersensitive State**
J. E. HOWARD, A. M. HARVEY, R. A. CAREY, and W. L. WINKENWERDER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1347–1349, Dec. 16, 1950. 7 refs.

The effects of adrenocorticotrophin (ACTH) and cortisone in 23 cases of asthma, 5 of serum sickness due to penicillin, 2 of sympathetic ophthalmia, and 2 of atropine sensitivity are described. The ACTH was usually given in doses of 100 mg. daily, diminishing gradually after 2 days to 20 mg., in 4 divided doses. The course lasted 6 to 21 days, the total dose ranging from 193 to 1,248 mg.

Only 4 of the 19 chronic asthmatics so treated were not completely relieved, and 2 of these were given, in error, only half the above dose. Relief lasted from 3 to 263 days, the smaller doses on the whole giving least relief. When the asthma recurred it is claimed that it was less severe than before treatment, and 6 patients received a second course with as much relief as after the first. The eosinophil count tended to fall from the 2nd to 7th days, but rose later when the dose of ACTH was below 30 mg. daily. Skin test reactions were reduced in severity and nasal mucosae appeared improved. Five patients with asthma who were given cortisone, 200 mg. daily for one day and then 100 mg. for 7 days, did not do well, only one with mild disease being relieved. Subsequently 3 of these patients responded to ACTH.

Four patients with penicillin reactions improved within 12 hours, and the symptoms had disappeared after 72 hours with ACTH in doses of 50 to 100 mg. daily to a total of 145 to 635 mg. On the other hand, cortisone did not entirely relieve the symptoms in another case. Atropine sensitivity was relieved in 2 cases, and improvement is also claimed in 2 cases of sympathetic ophthalmia [though the details given are meagre].

[Further details of the type of asthma in these cases would be welcome; a fuller account is to be published later.] *K. Gurling*

1943. **The Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Drug Hypersensitivity Reactions**
R. A. CAREY, A. M. HARVEY, J. E. HOWARD, and P. F. WAGLEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 354–386, Nov., 1950. 5 figs., 15 refs.

Five patients who were penicillin-sensitive (manifested by urticaria and angioneurotic oedema and, in 2 of the patients, by fever and arthritis) responded dramatically to the administration of 50 to 100 mg. daily for from 3 to 9 days of adrenocorticotrophic hormone (ACTH). Improvement was noted within a few hours and was complete in 1 to 5 days. Response was slower and less complete in another patient given 200 mg. of cortisone daily for 4 days. In 4 of the 6 patients minor relapses occurred 5 to 14 days after treatment was stopped. In 1 of the patients receiving ACTH there was only a minimal reaction to a further injection of penicillin.

ACTH, 100 mg. daily, was given to a patient who was sensitive to iodine (high fever, angioneurotic oedema, buccal ulceration, and exfoliative dermatitis). He responded within 48 hours, resolution being complete within 4 days. Although treatment was continued for 8 days, the condition relapsed 6 days later; it again responded to ACTH, this time permanently.

In 2 patients who reacted to local application of atropine to the eye (oedema of the eyelids and cornea and dermatitis of the face) there was a rapid response to ACTH, 100 mg. daily; sensitivity to atropine was abolished, as shown by the patch test. One patient in whom there was an acute reaction to 3-hydroxy-2-phenylcinchoninic acid (HPC), given in the treatment of chronic lupus erythematosus, received 200 mg. ACTH; resolution was rapid and there was no reaction to a further dose of HPC. An asthmatic patient who was sensitive to aspirin reacted only mildly to 130 mg. of aspirin during treatment with 140 mg. of ACTH daily and did not react to 80 mg. of aspirin after ACTH was discontinued. In 2 cases of hypersensitivity to sulphonamides (generalized skin eruption, stomal ulceration, and agranulocytosis) the leucocyte count returned to normal and there was some improvement in the skin condition. One of the patients, however, a man of 55, was receiving penicillin and aureomycin at the same time; the dosage of ACTH was inadequate and he subsequently died in uraemia. *Robert de Mowbray*

1944. **Constitution and Asthma.** (Konstitution und Asthma)
H. ARNOLDSSON and U. PIPKORN. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 437–448, Nov. 10, 1950. 3 figs., 26 refs.

METABOLIC DISORDERS

1945. **The Electrocardiogram and Disturbance of Potassium Metabolism**
J. H. CURRENS and J. D. CRAWFORD. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 843–850, Nov. 30, 1950. 7 figs., 29 refs.

The authors point out that the serum potassium level is not necessarily correlated with the degree of electrocardiographic abnormality found in disorders of potassium metabolism, and present 6 illustrative cases in patients admitted to the Massachusetts General Hospital. The diagnoses were: (1) nephrocalcinosis with "salt-losing nephritis" and potassium deficiency; (2) sprue with potassium deficiency; (3) hypopituitarism and adrenal insufficiency, with potassium deficiency following therapy; (4) terminal potassium deficiency and hypocalcaemia after transplantation of ureters [for unspecified reasons]; (5) adrenocortical virilism and Addison's disease, with potassium intoxication; and (6) Addison's disease and hypoparathyroidism, with potassium deficiency after testosterone therapy. In cases (1) and (2) tracings suggestive of potassium deficiency were obtained

at times when the serum potassium level was normal, although in case (1) the patient had muscular paralysis due to potassium deficiency at the time. In case (3), while potassium was being administered intravenously the serum level rose to more than double the normal figure, though the electrocardiogram was normal. In case (4) T waves were broad and upright while the serum potassium and calcium levels were very low; there was slight depression of the ST segments and some prolongation of systole which might have been due to lack of potassium or calcium. In case (5) an electrocardiographic diagnosis of potassium intoxication was valuable at a time when the serum level could not be estimated. In case (6) a virtually normal electrocardiogram was found in the presence of a very low serum potassium level.

It is inferred that the electrocardiogram reflects changes in the intracellular potassium concentration which do not necessarily run parallel with changes in the serum level, the latter being affected by fluctuations in the rates of absorption or excretion of potassium or of its take-up by the cells. In the absence of any simple means of estimating intracellular potassium, the electrocardiogram is recommended as a simple and useful guide.

J. A. Cosh

1946. **Vitamin-B Complex and Extract of Gastric Mucosa in the Treatment of Pellagra and Other Tropical Nutritional Disturbances.** (El complejo B y extracto de mucosa gastrica en pelagra y otros trastornos nutritivos de los paises tropicales)
E. MARTÍ PRIETO. *Revista Cubana de Pediatría* [*Rev. cubana Pediat.*] **22**, 653–705, Nov., 1950. 10 figs., bibliography.

The author discusses previous work on the aetiology and pathology of pellagra, the roles of nicotinic acid and the vitamin-B complex in this condition, and the important part played by the liver in nutritional disturbances of this type. He then discusses the therapeutic action of extract of gastric mucosa and of vitamin-B complex in this and other nutritional deficiencies such as sprue, the steatorrhoeas, nutritional oedema, and infantile dystrophies. Detailed histories are given of 10 infants with predominantly pellagra-like symptoms, 5 of whom were treated with extract of gastric mucosa and 5 with vitamin-B complex. Clinical cure was obtained in both groups, although the liver histology (as shown in photomicrographs of liver biopsies) did not always return to normal.

René Méndez

1947. **Pellagra in Fiji**
S. G. ROSS. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 921–928, Nov., 1950. 8 refs.

1948. **The Electrophoretic Serum-protein Pattern in Malignant Malnutrition**
C. G. ANDERSON and A. ALTMANN. *Lancet* [*Lancet*] **1**, 203–204, Jan. 27, 1951. 11 refs.

The electrophoretic examination of sera, taken at various stages during treatment, from Bantu children suffering from malignant malnutrition or from nutritional oedema has shown that, although on admission to hospital the total serum-protein content is much below normal values, the amount of γ-globulin is both absolutely and relatively normal or higher than normal. The albumin content is much reduced whilst the values for α- and β-globulins are about normal. After clinical cure the albumin content of the serum is usually still below normal and the γ-globulin considerably above normal. The abnormal γ-globulin content may persist for at least a year with the patient in good condition and on an adequate diet. These findings are similar to those found in adults with "hunger disease" and therefore link malignant malnutrition to the hunger oedema of adults.—[Authors' summary.]

1949. **Post-traumatic Paroxysmal Hyperinsulinism.** (О посттравматическом пароксизмальном гиперинсулинизме)
I. K. ZUZIN. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 4, 31–34, 1950.

A case of spontaneous hyperinsulinism, which developed in a woman of 48 after repeated cerebral trauma, is described. Attacks of hypoglycaemia could be provoked by psychological upset or physical strain, and by giving minute doses of glucose or sweets. Local disease of the pancreas was thought to have been excluded by clinical observation and the appropriate tests.

L. Crome

1950. **Familial Hemochromatosis: with Comments on Adrenal Function in Hemochromatosis**
W. F. ROGERS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 530–537, Nov., 1950. 4 figs., 17 refs.

Haemochromatosis is rare, although it is possibly missed in clinical examination from time to time, and there are few cases on record of the occurrence of the malady in siblings. The present report is of a pair of brothers who exhibited all the clinical features of the disease. Very full clinical, biochemical, and histological reports are given with some commentary on the deposition of the haemosiderin in the suprarenal capsules. The relationship between the deposition of haemosiderin in the suprarenal capsules and the pigmentation which is such a feature of haemochromatosis is briefly discussed, but an elucidation of the processes concerned is not forthcoming.

G. F. Walker

1951. **Milkman's Syndrome in Idiopathic Steatorrhoea Complicated by Refractory Macrocytic Anaemia**
A. ANDERSON. *Lancet* [*Lancet*] **2**, 897–900, Dec. 30, 1950. 14 refs.

The case is described of a patient who, in 1942, had a macrocytic anaemia, resistant to liver treatment, for which no cause was found at that time. In 1946 she was still anaemic and bone pains were now present. *X*-ray examination showed pseudo-fractures, and a diagnosis of osteomalacia secondary to idiopathic steatorrhoea was confirmed by fat-balance studies. She had not had diarrhoea, and the importance of examining fat balance in this type of patient is emphasized. The author also discusses the differential diagnosis of

macrocytic anaemia, and Albright's views on the pathogenesis of osteomalacia are summarized.

D. A. K. Black

1952. Effects of Cortisone and Adrenocorticotrophic Hormone (ACTH) on Experimental Scurvy in the Guinea Pig

G. A. HYMAN, C. RAGAN, and J. C. TURNER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 470–475, Nov., 1950. 2 figs., 22 refs.

In experiments carried out at Columbia University, New York, the effects of cortisone and adrenocorticotrophin (ACTH) were studied on scorbutic guinea-pigs approximately 2 months old and weighing 300 to 400 g. In the first experiment 2 animals received 12·5 mg. of cortisone subcutaneously daily for 13 days before the scorbutic diet was started and 3 received the same dosage of cortisone only after the diet had been given for 10 days, while 5 were not treated. In the second experiment 4 animals were given cortisone as above after 10 days on the scorbutic diet, 4 received 6·25 mg. of ACTH subcutaneously every 6 hours after 10 days on the same diet, while a third group of 4 animals were untreated.

The results of these two experiments are considered together. In 9 untreated controls, bloody diarrhoea and haematuria developed on the 10th to 12th day after starting the scorbutic diet in all animals, while hind-leg paralysis, tachypnoea, and abdominal distention developed in 5. The average duration of life was 21·9 days with a range of 20 to 24 days. Marked haemorrhages in the subcutaneous tissues and organs were seen post mortem. The 2 animals receiving cortisone for 13 days before beginning the diet died after 22 and 24 days' diet respectively. In those receiving cortisone after 10 days' diet clinical scurvy was approximately one week later in onset and appeared less severe than in the untreated controls. Similar results were noted in the guinea-pigs receiving ACTH. Glycogen was not demonstrable histochemically in sections of the liver, adrenal, or muscle of the controls, but small amounts were present in each of these tissues in those animals receiving ACTH or cortisone. The adrenal glands of the control animals were considerably hypertrophied and the ascorbic acid content was too low to be measurable (<2·5 μg. per 100 g.). In those given cortisone the adrenals were hypertrophied, but less so than in the controls; the ascorbic acid content in most cases was too low to be measurable. The greatest adrenal hypertrophy occurred in the ACTH-treated group, the ascorbic acid content again being too low to be measurable.

The conclusion is reached that cortisone and ACTH can prolong life and reduce the severity of scurvy induced in animals by deprivation of ascorbic acid, the effects of the two hormones being similar, so that ascorbic acid does not appear to be needed for the production of corticosteroids similar to cortisone by the adrenal cortex. The locus of action of corticosteroids in reducing haemorrhagic manifestations is not clear, and may be in the blood vessels or perivascular tissues. In an addendum based on further experience the authors remark that with these relatively high doses of cortisone and ACTH severe toxic effects may mask the protective effects. Hyperadrenalism, however, is found in all the treated scorbutic animals.

Norval Taylor

1953. Response to Adrenocorticotrophic Hormone in Clinical Scurvy

H. S. TREAGER, G. J. GABUZDA, N. ZAMCHECK, and C. S. DAVIDSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 517–520, Nov., 1950. 9 refs.

At the Boston City Hospital, 4 patients with clinical and laboratory evidence of scurvy received test doses of adrenocorticotrophin (ACTH) before and after the administration of therapeutic amounts of ascorbic acid. A normal eosinophil response was obtained in all cases and the response was unchanged after giving ascorbic acid. The blood glutathione and serum sodium and potassium concentrations fell within the normal range, thus providing confirmatory evidence of normal adrenal cortical function. Estimation of urinary excretion of uric acid after ACTH was impracticable because of low urine volumes; this was probably due to contaminating antidiuretic activity. It is concluded that either ascorbic acid is not necessary for normal adrenal cortical function, as measured by the above tests, or that there was residual ascorbic acid in the adrenal glands of these patients, despite its absence from the blood.

Norval Taylor

DIABETES

1954. Spontaneous Hyperpotassemia as a Cause of Death in Diabetic Acidosis

R. A. NEUBAUER and R. W. FRELICK. *American Heart Journal* [*Amer. Heart J.*] **40**, 793–797, Nov., 1950. 1 fig., 29 refs.

The authors report a rapidly fatal case of diabetic coma precipitated by heat. The electrocardiographic diagnosis of hyperpotassaemia was confirmed post mortem, the blood taken from the ventricle 1 hour after death containing 14 mEq. of potassium and 96 mEq. of sodium per litre. It is assumed that the early and rapidly progressing shock with severe dehydration and decrease in serum sodium content reduced glomerular filtration to such an extent that the serum potassium concentration rose to fatal levels.

A. Schott

1955. Lessons for Future Treatment from 472 Fatalities in Diabetic Children

E. P. JOSLIN and J. L. WILSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1293–1296, Dec. 9, 1950.

Of the 2,873 diabetic children under 15 years of age seen by the senior author since 1898, 472 had died by December, 1949, only 20 patients being untraced. The causes of death in the various eras of treatment are analysed. Coma accounted for 86% in the pre-insulin era, but for only 8·6% in the last 6 years, whereas deaths from tuberculosis have risen from 0 to 11·2% because the patients have lived long enough to develop it in early adult life. Both these causes of death are largely

preventable, but very few of those who died of them had been seen or treated by the Boston group for years, and none in their terminal illness, otherwise their deaths might possibly have been prevented.

In the last 6 years 51·9% of deaths were due to renal complications—the Kimmelstiel–Wilson syndrome of albuminuria, hypertension, and uraemia. The authors state that " the early signs and symptoms for which we must be ever alert, and for which prophylaxis and *newer therapeutic aids may be helpful*, are those of complications in the kidney ". [No reasons are given for the optimism of the words the abstracter has italicized.]

R. D. Lawrence

1956. **Progress Notes on Fifty Diabetic Patients Followed Twenty-five or More Years**

R. E. Reuting. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 891–897, Dec., 1950. 1 ref.

A follow-up report is presented on a group of 50 patients originally selected for special study of the aetiology of vascular complications in diabetes in 1929 and reported on by Shepardson in 1930. In the 31 surviving in November, 1949, the average duration of the disease was 28·4 years. All were actively leading a normal life except one who had a neurosis.

Of the 19 deaths, cardiovascular and renal disease accounted for 7, diabetic coma for 1, pulmonary tuberculosis for 4, and other infections for 4. Three patients died of causes unrelated to diabetes. Necropsy on one patient dying of coronary disease showed pulmonary tuberculosis with caseation which had not been demonstrable by *x* rays. No patient developed gangrene. Of the 31 survivors, some retinopathy was present in 18, and in 27 arterial calcification was radiologically demonstrable. Eight showed evidence of nitrogen retention and 9 had albuminuria exceeding 20 mg. per 100 ml. The lowest plasma cholesterol level was found in a patient with marked vascular calcification. The blood pressure was normal in 15 of 28 survivors recently examined, the average for the whole group being 142/83 mm. Hg.

The author considers that with modern treatment of infections the over-all death rate would have been reduced from 36 to 22%, the major persisting cause of death in diabetes being cardiovascular–renal disease.

C. L. Cope

1957. **Polyvinylpyrrolidone as a Means of Delaying the Absorption of Insulin.** (Il polivinilpirrolidone come ritardante l'assorbimento dell'insulina)

M. Balduini and E. Granata. *Riforma Medica* [*Rif. med.*] **64**, 1303–1308, Dec. 2, 1950. 4 figs., 24 refs.

Polyvinylpyrrolidone (PVP) has been used to delay the absorption of various therapeutic substances; it appears also to delay renal excretion, and in the case of hormones may temporarily inhibit the action of proteolytic enzymes. Combined with insulin, it results in a stable and homogeneous solution which is easily sterilized and well tolerated.

When given to 4 normal subjects by the authors, insulin-PVP caused a prompt and prolonged fall in blood sugar level for 12 to 18 hours, but without the extreme hypoglycaemic effect of soluble insulin. The blood sugar level in 4 mild cases of diabetes remained normal throughout the whole 24 hours after a single subcutaneous injection in the morning, and glycosuria disappeared entirely. In 4 moderate or severe cases the maximum fall in blood sugar level occurred 4 hours after the morning dose, the level remaining within normal limits throughout the day so that no more insulin was required. Moreover the optimum dose of insulin-PVP was less than that of other insulins used previously. However, in the severest cases an additional dose of soluble insulin may be necessary. The intake of carbohydrate was arranged so that 50 to 60% of the total was given at breakfast and the rest spaced equally throughout the day. A hypoglycaemic reaction occurred in one case, but this was attributed to idiosyncrasy.

A. Paton

1958. **Studies of the Inheritance of Diabetes Mellitus. I. The Relation of Heredity and the Age of Onset of Diabetes**

M. W. Thompson, L. E. Laakso, and E. M. Watson. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 556–559, Dec., 1950. 3 figs., 7 refs.

Family histories were obtained of 1,380 patients with diabetes mellitus in Ontario through personal interviews, from hospital records, and by questionnaire. A " positive family history " of diabetes was found in 50% of females and 51% of males. The percentage decreased steadily with increasing age of onset in males, from 70% when onset was in the first decade to 30% in the 8th decade. The trend in females was similar except for an unusually low proportion of positive family histories where onset was in the 2nd decade. Where the positive family history was bilateral the mean age of onset was 33·1, where unilateral 47·3, and where negative 53·8 years.

The authors conclude that diabetes mellitus behaves genetically as a graded character and that their findings conflict with the view that juvenile diabetics are homozygous and older diabetics heterozygous for a gene predisposing to diabetes.

[No definition of the term " positive family history " is given. It is not possible to read from the graphs shown the numbers on which the percentages quoted are based, since men and women are not shown separately on the graph of distribution of patients by age of onset. The bearing of this investigation on the genetics of diabetes is so indirect, and so many qualifying factors are present, that only tentative conclusions may be drawn.]

C. O. Carter

1959. **Detection of Diabetes in a Nutrition Survey—A Study of 550 Persons in Ottawa County, Michigan**

E. C. Tabor and K. H. Frankhauser. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 1330–1335, Oct. 13, 1950. 9 refs.

See also Section Cardiovascular Disorders, Abstract 1974.

Cardiovascular Disorders

1960. **Anticoagulant Therapy with Heparin in Pitkin's Menstruum**
J. F. GOODWIN and A. G. MACGREGOR. *Lancet* [*Lancet*] 2, 667–671, Dec. 2, 1950. 4 figs., 16 refs.

The authors treated 24 patients with thrombo-embolic disease (venous thrombosis in 8; myocardial infarction in 6; pulmonary embolism in 9; and arterial embolism in 1) with heparin in Pitkin's menstruum (heparin *B.P.*, 200 mg., gelatin *B.P.*, 360 mg., dextrose *B.P.*, 160 mg., acetic acid *B.P.*, 0·03 ml., water to 2 ml.). At room temperature this preparation forms a solid gel and must be warmed to body temperature for injection. The mixture was drawn into the syringe followed by 1 ml. of 2% procaine and the whole slowly injected into a large muscle mass. Subcutaneous injections were found to be unsatisfactory. Two daily injections of from 2 to 4 ml. proved necessary. In all but 3 of the cases a satisfactory prolongation of the coagulation time was achieved, but as this took 6 to 24 hours soluble heparin was given at the start in cases where an immediate response was necessary. Sometimes absorption was erratic and there was an occasional sudden release of a large amount of heparin. Although, in such cases the coagulation time may be rapidly lowered by the injection of 5 ml. of 1% protamine sulphate, it is clear that the method should be used only where there are adequate facilities for estimating the coagulation time.

In nearly every case bruising occurred at the site of injection and in 6 cases this necessitated stopping the treatment. In 2 cases there was severe bleeding at the site of injection, with considerable blood loss.

C. Bruce Perry

1961. **Activity of Heparin in Pitkin's Menstruum**
J. D. MUIR. *Lancet* [*Lancet*] **2**, 671–672, Dec. 2, 1950. 2 figs., 2 refs.

Heparin in Pitkin's menstruum was given by deep subcutaneous injection to 6 volunteers in doses of 300 mg. In 9 hours the coagulation time in 5 subjects was prolonged to 15 to 30 minutes, but in one the effect was much greater and lasted for 21 hours. The coagulation time could be promptly reduced by the injection of 10 ml. of 1% protamine sulphate. Ten patients with thrombo-embolic disease were treated satisfactorily with this preparation, receiving an initial dose of 400 mg. subcutaneously. The subsequent dosage varied from 200 mg. a day to 400 mg. twice a day according to the coagulation time. In urgent cases it was necessary to use aqueous heparin intravenously at the same time as the first subcutaneous injection of the heparin in Pitkin's menstruum, and sometimes this had to be repeated after 3 hours. Beyond slight discomfort at the site of the injection no untoward reaction occurred.

C. Bruce Perry

1962. **Electrocardiographic Effects of Arterenol and Isopropylarterenol in Man, with a Note on the Auricular T Wave**
A. LITTMAN, M. I. CROSSMAN, R. M. GUNNAR, J. H. ISAACS, J. H. HIRSCHMANN, and E. F. FOLEY. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 235–242, Nov., 1950. 4 figs., 14 refs.

In 4 healthy young adults the influence of " isopropylarterenol " (isopropyl-noradenaline, " isoprenaline ") and " arterenol " (noradrenaline) on the cardiovascular system was investigated. Within 1 to 2 minutes of the subcutaneous injection of 0·25 mg. of isoprenaline palpitations, frontal headache, and substernal oppression developed. The pulse rate rose to about 120, the diastolic pressure—as determined by auscultation—fell to zero, and the systolic pressure rose a little. In the electrocardiogram there was a depression of the S–T segment, greatest in leads II and III, and the QRS complex lay in a trough-like configuration which suggested augmentation of the auricular T waves. All these changes began to disappear after 30 minutes and had almost disappeared after one hour. In contrast, 1 to 2 mg. of DL-noradrenaline caused a rise in the systolic pressure by 22 to 46 mm. and in diastolic pressure by 20 to 26 mm. Hg, with a slowing of the pulse rate by 20 to 24 beats. There was some headache, but no electrocardiographic change. When 2 or 4 mg. of noradrenaline was given at the time of maximum action of isoprenaline, a reversal of its effects occurred: pulse rate and diastolic pressure returned to normal, and systolic pressure became hypertensive. The electrocardiographic changes, however, persisted. Noradrenaline given after 2 to 6 mg. of atropine caused tachycardia and the same electrocardiographic changes as with isoprenaline. As the electrocardiographic changes do not seem to depend on the presence of tachycardia it is assumed that there is a direct myocardial action by both isoprenaline and noradrenaline. *H. Herxheimer*

1963. **Electrocardiographic Studies at Angiocardiography**
G. BIORCK, T. SYLVAN, and G. LINDBLOMTILLMAN. *Acta Cardiologica* [*Acta cardiol., Brux.*] **5**, 509–520, 1950. 2 figs., 8 refs.

When an opaque medium is injected for purposes of angiocardiography at a pressure of several atmospheres, the velocity at which the fluid leaves the catheter may exceed 30 m. per second. Experiments have shown that in the cadaver the injected fluid may pass into, or even cut through, the dead heart muscle. In patients such high speeds of injection are not used. Nevertheless it is important to determine by simultaneous electrocardiography if the heart action is disturbed by the injection of a contrast medium and, if so, which parts of the heart are particularly liable to such disturbances, or which malformations are most susceptible.

In the present investigation, 48 consecutive patients were examined, 32 being males and 16 females. The youngest was 8 years old and the oldest 58 years. In most cases a 50 to 70% solution of "umbradil" was used; occasionally diodone was chosen. Velocities of less than 30 m. per second were used. A modified CR_5 lead was used and the *x*-ray exposure recorded automatically on the electrocardiographic film. Disturbances of heart rate or rhythm were almost constant findings. "Coronary" (repolarization) changes were occasionally noticed in aortograms when the catheter was either mistakenly occluding, or placed very close to, the opening of a coronary artery. Premature beats of all kinds, including so-called left ventricular premature beats, were produced in 20 of 22 cases when the catheter was in the right heart or pulmonary artery. The pacemaker mechanism and intracardiac conduction were often less affected. The disturbances induced by the injection soon disappeared in all cases, as judged by check electrocardiograms taken a few days afterwards.

F. A. Langley

1964 (*a*). **The Left Intraventricular Potential of the Human Heart. I. Method**
D. Sodi-Pallares, A. Estandía, J. Soberón, and M. I. Rodríguez. *American Heart Journal* [*Amer. Heart J.*] **40**, 650–654, Nov., 1950. 5 refs.

The left intraventricular potential was studied in 25 persons, including normal and hypertensive subjects and patients with aortic incompetence (syphilitic and rheumatic). The method consisted in the introduction into the radial artery (preferably on the right side) in the region of the cubital fossa of a ureteric catheter with a fine silver wire in the lumen, and its passage into the left ventricle. The technique is described in detail. Three anatomical obstacles are usually encountered: at the level of the clavicle, at the beginning of the brachiocephalic trunk, and at the aortic valves; the technique of their management is described. Untoward effects were: passage of the catheter into the right coronary artery, induction of arrhythmia, and, with prolonged procedure, acute pain in the cubital fossa. There was one death 3 days after catheterization. In several subjects both ventricular cavities were simultaneously catheterized, the tips of both catheters placed at the same level of the interventricular septum, and trans-septal bipolar leads recorded. *A. Schott*

1964 (*b*). **The Left Intraventricular Potential of the Human Heart. II. Criteria for Diagnosis of Incomplete Bundle Branch Block**
D. Sodi-Pallares, A. Estandía, J. Soberón, and M. I. Rodríguez. *American Heart Journal* [*Amer. Heart J.*] **40**, 655–679, Nov., 1950. 28 figs., 15 refs.

The main criterion for the diagnosis of incomplete left bundle-branch block by means of the left intraventricular cavity lead (see Abstract 1964 (*a*)) consists in the presence of an initial positivity, which indicates activation of the interventricular septum from right to left. This diagnosis can be detected also in the presence of slurring at the beginning of the ascending limb of the R wave in those leads which reflect the potentials of the left ventricle, that is, most frequently leads I, V_L, V_5, and V_6. Absence of the Q wave in these leads supports the diagnosis, but their presence does not exclude it. The duration of the QRS complex is considered unimportant, since the diagnosis can be made even if this is less than 0·10 second.

The authors suggest that some records interpreted as denoting the Wolff–Parkinson–White syndrome may actually indicate left bundle-branch block. In some cases it was found necessary to catheterize both ventricles and record transseptal leads in order to make the diagnosis. It is tentatively suggested that ventricular hypertrophy without block is less frequent, and that block, with or without hypertrophy, far more frequent, than is commonly thought, but catheterization of both ventricles "in a great many patients" will be necessary to clarify this point. *A. Schott*

1965. **The Ventricular Electrokymogram**
L. C. Akman, A. J. Miller, E. N. Sibler, J. A. Schack, and L. N. Katz. *Circulation* [*Circulation*] **2**, 890–899, Dec., 1950. 8 figs., 17 refs.

In 32 young, healthy adults, over 200 electrokymographic tracings of the left ventricle were obtained, the heart sounds being recorded simultaneously by means of a stethocardiograph for purposes of time reference. On the average six different sites over the left ventricle were explored in each case; the curves obtained were analysed and compared. The authors present in two tables the relevant measurements and the range of variation as between one tracing and another in the same individual. The contour variations are described in detail and illustrative examples reproduced.

It is concluded that variations in contour and time sequence of events in the normal electrokymogram are considerable. These variations are caused not so much by changes in cardiac volume as by positional movements of either the whole or parts of the heart. Furthermore it was found that there was no consistent moment-to-moment time relationship between electrokymograms obtained at various sites on the left ventricular border and the heart sounds.

It is pointed out that certain curve patterns hitherto described as abnormal and characteristic of myocardial infarction and constrictive pericarditis might occur as a normal variant in electrokymograms from healthy hearts. *A. I. Suchett-Kaye*

1966. **Correlation of Simultaneously Recorded Electrokymograms and Pressure Pulses of Human Heart and Great Vessels. A Preliminary Report.**
A. H. Salans, J. A. Schack, and L. N. Katz. *Circulation* [*Circulation*] **2**, 900–906, Dec., 1950. 8 figs., 14 refs.

This study was undertaken to investigate further the meaning of the deflections on the electrokymographic tracing. For this purpose electrokymograms were obtained from the right ventricle, right auricle, pulmonary artery, and superior vena cava, pressure curves from the corresponding cavities and great vessels being simultaneously recorded. This necessitated concurrent

right-heart catheterization and electrokymography of the cardiac silhouette. Six patients were investigated in this manner.

The border electrokymograms from the pulmonary artery and superior vena cava showed " a remarkable constancy of time relationship with simultaneous intraluminal pressure curves ". The " densograms " (density electrokymograms) obtained from the same areas followed with a somewhat greater variation.

The border electrokymogram from the right ventricle was less easy to analyse because it was more difficult to define the exact points on these tracings as compared with those of the great vessels.

The authors end their communication with the warning that until more is known of the physiological basis of these tracings, " clinical applications must be approached with great caution ". *A. I. Suchett-Kaye*

1967. **Spatial Vector Electrocardiography. A Method for Calculating the Spatial Electrical Vectors of the Heart from Conventional Leads**
R. P. GRANT. *Circulation* [*Circulation*] **2**, 676–695, Nov., 1950. 4 figs., 13 refs.

1968. **Electrocardiographic Patterns in Stokes–Adams Syndrome**
B. H. PASTOR and S. H. WORRILOW. *Annals of Internal Medicine* [*Ann. intern. Med.*] **34**, 80–89, Jan., 1951. 5 figs., 26 refs.

HEART

1969. **The Occurrence of Renal Insufficiency in Subacute Bacterial Endocarditis**
H. VILLARREAL and L. SOKOLOFF. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 655–661, Dec., 1950. 1 fig., 16 refs.

In a series of 100 cases of subacute bacterial endocarditis which terminated fatally there were 14 cases of uraemia, with non-protein nitrogen levels in the blood varying from 75 mg. to 224 mg. per 100 ml. At necropsy on these patients with uraemia, 8 cases showed embolic glomerulonephritis, 1 case a combination of embolic and chronic diffuse glomerulonephritis, 1 case a combination of embolic glomerulonephritis and an unclassified type of nephritis, while 3 cases showed a typical picture of chronic glomerulonephritis and one that of subacute glomerulonephritis. The findings demonstrate that uraemia is by no means an infrequent complication of subacute bacterial endocarditis. *G. Cardikas*

1970. **Increasing Bacterial Resistance to the Antibiotics. A Study of 46 Cases of Streptococcus Endocarditis and 18 Cases of Staphylococcus Endocarditis**
D. C. LEVINSON, G. C. GRIFFITH, and H. E. PEARSON. *Circulation* [*Circulation*] **2**, 668–675, Nov., 1950. 5 refs.

The treatment with antibiotics of 46 patients with bacterial endocarditis caused by a streptococcus and of 18 with staphylococcal endocarditis is reported. In 20% of the streptococcal and in 66% of the staphylococcal cases the infecting organism was found to be relatively penicillin-resistant. The authors recommend that such cases be treated with up to 20 million units of penicillin daily for at least 6 weeks. Aureomycin was used in 3 penicillin-resistant cases with some success in 2 of them, aureomycin resistance developing in the third. *H. E. Holling*

1971. ***Candida* and *Aspergillus* Endocarditis. With Comments on the Role of Antibiotics in Dissemination of Fungus Disease**
L. E. ZIMMERMAN. *Archives of Pathology* [*Arch. Path.*] **50**, 591–605, Nov., 1950. 5 figs., 27 refs.

Three cases of disseminated fungus infection are reported in this paper. The first case was that of a woman aged 38 who was admitted to hospital with a history suggestive of acute endocarditis. A species of *Candida*, identified as *C. guilliermondi*, was isolated from the blood. After an illness of some 4 weeks the patient died and post-mortem examination showed a large, fungating vegetation involving about two-thirds of the circumference of the mitral valve. Sections showed evidence of underlying old rheumatic disease, while the entire bulk of the new deposit consisted of fungal mycelium and an abundance of spores.

In the second case a 25-year-old male had sustained injuries to one leg. Amputation below the knee was carried out and penicillin given, but the stump remained oedematous, foul-smelling, and semi-necrotic. Amputation above the knee was therefore proceeded with. Low-grade fever persisted, however, and a month later a to-and-fro murmur could be heard over the entire precordium. The patient died about a fortnight later and post-mortem examination showed very large vegetations on the aortic valve and adjoining mural endocardium. Microscopically, the vegetation was composed of a massive fungal growth showing the typical lateral branching of *Aspergillus*. The third case was that of a 32-year-old woman who had attacks of pyrexia of undetermined origin. Later, precordial murmurs were heard and penicillin and streptomycin were given, but without response. At necropsy the heart showed evidence of old rheumatic disease with, in addition, friable, greyish vegetations on the aortic valve. Microscopically, small spores were seen, identified as *Histoplasma capsulatum*. Branching septate hyphae were also found, indicating *Aspergillus* infection.

The author points out that typical *Candida* and *Aspergillus* organisms are easily recognized, but difficulty arises when mycelial elements are not visible or are not recognized. Further, variations in size, branching, and septation are complicating factors. With regard to causal factors, cases are quoted in which treatment with antibiotics for bacterial infection has apparently caused dissemination of fungus disease. It is possible that antibiotic drugs have a growth-enhancing effect on fungi, or possibly a growth-restraining substance normally produced by the natural bacterial flora of the intestine is lacking after such treatment. Other possible factors include bone-marrow depressants, since oropharyngeal moniliasis is frequent in patients receiving anti-folic-acid drugs. *R. B. Lucas*

1972. **Chloramphenicol in Subacute Bacterial Endocarditis**
M. CURTIN. *Lancet* [*Lancet*] **2**, 804–805, Dec. 16, 1950. 1 fig., 1 ref.

1973. **Subacute Bacterial Endocarditis caused by *Gaffyka tetragena*. Report of a Case**
R. D. BOYNTON. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 738–740, Nov. 9, 1950. 1 fig., 24 refs.

1974. **Myocardial Degeneration due to Insulin.** (Die Insulin-Myokardose)
K. AKERT. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1010–1015, Sept. 16, 1950. 6 figs., bibliography.

A man aged 39 with schizophrenia had been treated for a long time with insulin, and died 3 hours after the injection of 140 units of insulin from sudden cessation of cardiac action. Necropsy revealed sarcolytic myocardosis (absence of muscle fibres), an unusual type of hepatic lobular cirrhosis, and multiple ulcers of stomach and duodenum. The endocrine glands showed changes ascribed to an anti-insulin reaction, such as eosinophilia in the anterior pituitary, hyperplasia of the suprarenal cortex with atrophy of the medulla, and hyperplasia of the α-cells of the pancreatic islets.

N. Policzer [*Excerpta Medica*]

1975. **Myocarditis in Acute Infectious Diseases. A Clinical and Electrocardiographic Study**
I. FINE, H. BRAINERD, and M. SOKOLOW. *Circulation* [*Circulation*] **2**, 859–871, Dec., 1950. 7 figs., bibliography.

Of a group of 84 patients suffering from one or another type of acute infectious disease, 28 had abnormal electrocardiograms as compared with their own normal control records. Serial electrocardiographic studies were necessary to demonstrate some of the abnormalities, and the unipolar and V leads were of undoubted value sometimes in revealing abnormal T waves when such changes were not seen in standard leads. Abnormal T waves were present in 20 patients, prolongation of the P–R interval in 8, significant RS–T deviation in 3, and abnormalities of rhythm in 6. Prolongation of the QRS interval was observed in only 4 patients. Abnormalities of conduction and rhythm occurred chiefly in the patients with diphtheritic myocarditis.

The majority of electrocardiographic changes occurred within the first 10 days of the illness. In scarlet fever and acute streptococcal throat infections changes, if any, normally appeared within 1 or 2 days after onset and seldom persisted for more than a day or two. In typhoid fever the abnormalities usually appeared during the 2nd or 3rd week. On the whole, any deviations noted from normal were evident during the febrile phase of the disease. The electrocardiogram eventually became normal in all the survivors.

Clinical manifestations of myocarditis were present in nearly all those with abnormal tracings. The most reliable clinical sign of myocardial damage was a first heart sound of poor quality at the apex. The others, in order of importance, were: a fall in systolic blood pressure of 20 mm. Hg or more, diastolic gallop rhythm, systolic murmur, and a pulse rate of 120 or over. Some of the patients had more than one physical sign of myocarditis. Eleven of the patients studied died and 4 came to necropsy; in these there was found histological confirmation of myocarditis (2 with diphtheria, 1 with typhoid fever, and 1 with miliary tuberculosis).

Patients undergoing artificial fever therapy did not show clinical or electrocardiographic signs of myocardial involvement.

It is concluded that the occurrence of myocarditis during an acute infectious disease is not of great prognostic significance except in diphtheria.

A. I. Suchett-Kaye

1976. **The Action of Cardiac Glycosides on Experimental Auricular Flutter**
A. FARAH and T. A. LOOMIS. *Circulation* [*Circulation*] **2**, 742–748, Nov., 1950. 5 figs., 18 refs.

The action of G-strophanthin, digitoxin, and lanatosid C was studied on the auricular flutter produced in dogs by the method of Rosenblueth and Garcia Ramos (*Amer. Heart J.*, 1947, **33**, 677). This method consists in the direct stimulation of the atrium at the rate of 15 to 20 impulses per second. Crushing a narrow band of tissue connecting the venae cavae ensures the production of a stable auricular flutter. This flutter, unlike that produced by aconite, is thought to originate in a circus movement.

In the normally innervated heart lanatosid C changed this flutter to fibrillation, and reversion to normal rhythm followed section of the vagus or atropinization. In the denervated heart the glycosides decreased the flutter rate and in some cases caused reversion to normal rhythm. This was thought to be due to a decrease in the conducting velocity of the auricular muscle. Failure of the auricle to follow the more rapid rates of stimulation after administration of the glycosides indicated an increase in the effective refractory period. It was concluded therefore that the actions of the vagus and the cardiac glycosides are antagonistic, the vagus decreasing the refractory period and increasing conduction velocity, whereas the cardiac glycosides have the opposite effect. The net result depends on the balance of these two actions.

H. E. Holling

1977. **Procaine Amide (Pronestyl) in the Treatment of Disorders of Cardiac Rhythm. Preliminary Report**
J. M. KINSMAN, H. L. CLAY, W. S. COE, and M. M. BEST. *Journal of the Kentucky State Medical Association* [*J. Kentucky med. Ass.*] **48**, 509–511, Nov., 1950. 1 fig.

The effect upon various arrhythmias of procaine amide, given intravenously in doses ranging from 200 mg. to 2,000 mg., was investigated in 34 patients. Ventricular ectopic beats were abolished in 10 out of 11 cases, paroxysmal ventricular tachycardia in 2, and auricular extrasystoles in 3 out of 4 patients. No effect was seen in persistent auricular fibrillation and flutter. Side-effects included transient flushing, fall of blood pressure,

and occurrence or aggravation of bundle-branch block. Further studies, including oral administration, of this drug are in progress. *A. Schott*

1978. **The Differential Diagnosis of Three Types of Congenital Heart Disease with Cyanosis.** (Differential-diagnose dreir Bilder von Morbus coeruleus)
K. KLINKE and H. SCHÄFER. *Kinderärztliche Praxis* [*Kinderärztl.Praxis*] **18**, 501–508, Nov.–Dec., 1950. 6 figs., 3 refs.

In 3 cases of congenital malformation of the heart the respective diagnoses of Fallot's tetralogy, Eisenmenger's complex, and transposition of the great vessels were made by evaluation of the clinical signs and symptoms only, with the support of simple tests such as determination of circulation time with fluorescein and of the oxygen saturation of the systemic arterial blood. The authors make the point that it is frequently possible to diagnose such cases and to assess the chances of successful operation by these simple methods without the aid of cardiac catheterization and angiocardiography.
W. Mestitz

1979. **Water and Electrolyte Balance during Recovery from Severe Congestive Failure on a 50 Milligram Sodium Diet**
L. T. ISERI, A. J. BOYLE, and G. B. MYERS. *American Heart Journal* [*Amer. Heart J.*] **40**, 706–730, Nov., 1950. 6 figs., 26 refs.

The effect of a diet containing only 50 mg. of sodium was studied in 7 patients with severe congestive heart failure which had proved refractory to the usual treatment. Of these, 4 had rheumatic valvular disease and 3 arteriosclerotic heart disease, with and without hypertension. Four patients (group I) had pulmonary congestion with peripheral oedema, and 3 (group II) had pulmonary congestion alone. The diet was given for periods ranging from 8 to 16 days. All patients showed a striking decrease in the clinical signs of congestion, and lost weight progressively. A fall in venous pressure and plasma volume and a rise in vital capacity were observed in those in whom determinations were made at the beginning and end of the experimental period. Water loss ranged from 8,150 to 14,160 ml. (11 to 17% of initial body weight) in patients of group I, and from 1,160 to 2,130 ml. (1·7 to 3·5%) in those of group II. The chloride loss ranged from 489 to 1,260 mEq. in group I, but in group II it was negligible or absent. In group I the external sodium balance was markedly negative (from −595 to −1,545 mEq.); in 2 patients of group II it was also negative (−101 and −164 mEq.), and in the remaining patient there was equilibrium. The intracellular potassium balance was positive in all cases, and sodium balance in all but one. In 6 a net cellular gain of nitrogen (3·7 to 33·9 g.) was found which was available for synthesis of protein.

The main biochemical changes associated with recovery from congestive failure in these cases thus consisted in intracellular loss of water and gain in sodium and potassium, this gain being regarded as the replenishment of a deficit caused by congestive failure. Rapid osmotic inactivation of cellular base has to be assumed for the purpose of maintaining osmotic equilibrium. These findings are in accordance with the view that the development of congestive heart failure is associated with a liberation of ionized base from osmotically inactive constituents of the protoplasm, with changes in the distribution of potassium, sodium, and water in the direction opposite to that observed during recovery.
A. Schott

1980. **Cation Exchange Resins in the Treatment of Congestive Heart Failure**
S. H. HAY and J. E. WOOD. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 1139–1149, Nov., 1950. 5 figs., 21 refs.

For many conditions of oedema and a variety of clinical maladies in which there is poor excretion of fluids it has long been the general custom to prescribe salt-free diets. Salt-free diet is all very well if it is enforced by the power and prestige of a hospital consultant staff and the authority of a hospital ward. Even so, and even in the best hospitals, a salt-free diet is trashy and insipid to most patients, and it is difficult to make it palatable. However much a patient may be impressed in a hospital, he often breaks away from his salt-free diet as soon as he gets home. Concerned with these well-known facts, the authors thought they might remove the difficulty by taking steps to ensure that salt was not absorbed from the stomach and intestine in the course of an ordinary diet. The device adopted was the giving with the diet of a resin, not so very unpalatable as it sounds, designed to fix and hold sodium and potassium and excrete both in the faeces. Biochemically the results seemed very successful in a series of 10 cases and the clinical reports obviously suggest further clinical experiments in conditions such as cirrhosis of the liver, nephritis, cardiac oedema, and any condition of salt retention. None of the patients seemed to come to any harm from ingestion of the resin, but all complained of gritty faeces.
G. F. Walker

1981. **Some Aspects of the Pulmonary Circulation in Normal Man and in Chronic Cardiopulmonary Diseases**
A. COURNAND. *Circulation* [*Circulation*] **2**, 641–657, Nov., 1950. 17 figs., 36 refs.

The author reviews the additions made in the past few years to our knowledge of the pulmonary circulation and reports certain personal observations in illustration. In 10 normal people the range of pressure in the pulmonary circulation was found to be: pulmonary artery, systolic 22±2·9 mm. Hg, diastolic 8±1·7 mm. Hg, mean 13±2·3 mm. Hg; pulmonary capillary pressure 5 mm. Hg. Pressure-pulse tracings from the pulmonary capillaries show two distinct positive waves, one of which is thought to be the forwardly transmitted pulmonary systolic pulse, the other the backwardly transmitted left atrial pulse. The latter disappears in auricular fibrillation.

In left ventricular failure there is a rise in the filling pressure of the left ventricle which is transmitted back through the lungs and results in an increased pulmonary arterial pressure. In diseases of the lung restriction of

the pulmonary vascular bed results in a rise of pulmonary arterial pressure, particularly under conditions such as exercise when the blood flow is increased. In chronic pulmonary emphysema the elevation of pulmonary arterial pressure shows some relationship to the degree of arterial oxygen saturation. Chronic anoxia due to lung disease leads to an increase in blood volume, polycythaemia, and in increase in cardiac output. These changes put an increased strain on the right heart, which hypertrophies and then fails. In 4 cases of emphysema of varying severity it was found that the more severely affected cases showed a smaller increase in cardiac output on exercise and a greater increase in pulmonary arterial pressure than the milder ones. In chronic lung disease therapy should be directed towards overcoming infection with antibiotics, and the relief of bronchiolar obstruction by the reduction of bronchial secretion and the use of atomized bronchodilators. *H. E. Holling*

1982. **A Synthetic Anticoagulant: a Polysulfuric Acid Ester of Polyanhydromannuronic Acid (Paritol). Experience with its Use in Man**
C. W. SORENSON and I. S. WRIGHT. *Circulation* [*Circulation*] **2**, 658–667, Nov., 1950. 1 fig., 9 refs.

A new synthetic anticoagulant, " paritol " (a polysulphuric acid ester of polyanhydromannuronic acid), was given in all to 35 subjects. In 15 patients with thrombo-embolic disorders the drug was used therapeutically, and in 16 other patients and in 4 normal subjects it was given merely to observe its effect. The anticoagulant effect of the drug was measured by a method modified from that of Lee and White and the prothrombin was estimated by the Link–Shapiro modification of the Quick one-stage method with dried rabbit-lung thromboplastin. The anticoagulant effect of paritol lasts 2 to 3 times longer than that of heparin. It must be given intravenously or unpleasant local reactions are caused. In a patient with kidney disease paritol seemed to cause a further increase in blood urea level. One patient suffered a vascular collapse as a result of taking the drug, and 2 had unusual swellings of the hands and feet. Further studies on the use of paritol in thrombo-embolic disease are required.
H. E. Holling

See also Section Pathology, Abstracts 1882–3; 1887; Section Neurology, Abstract 2104.

CORONARY ARTERY DISEASE

1983. **The Hypoxemia Test: an Analysis of 1,130 Tests.** [In English]
G. NYLIN, V. DE FAZIO, and F. MARSICO. *Cardiologia* [*Cardiologia, Basel*] **17**, 191–209, 1950. 4 figs., bibliography.

Electrocardiographic records were taken before and after breathing 9% oxygen in nitrogen on 1,103 subjects (1,130 tests in all). They were analysed along the lines suggested by Levy *et al.* (*Amer. Heart J.*, 1941, **21**, 634). In 31% of patients in whom angina pectoris was reasonably certain and 4·5% of patients with no suspicion of coronary disease positive results were obtained. It is suggested that the positive results in subjects without coronary disease may have been due to nervous or hormonal imbalance. *D. Verel*

1984. **Diet, Serum Cholesterol and Coronary Artery Disease**
M. M. GERTLER, W. M. GARN, and P. D. WHITE. *Circulation* [*Circulation*] **2**, 696–704, Nov., 1950. 2 figs., 36 refs.

The dietary history of 139 healthy males and of 90 who had suffered myocardial infarction before the age of 40 was investigated. There was no significant difference in the amount of cholesterol contained in the diets of the two groups, nor did the level of cholesterol in the serum appear to be related to the dietary intake. Judging by this study there appears to be nothing to be gained by restricting the intake of cholesterol-containing foods by patients with coronary artery disease.
H. E. Holling

1985. **The Treatment of Coronary Thrombosis and Fresh Myocardial Infarction with a New Anticoagulant Tromexan** [In English]
E. F. VON HUEBER. *Cardiologia* [*Cardiologia, Basel*] **17**, 223–233, 1950. 7 figs., 10 refs.

Twenty-one cases of recent myocardial infarction and 9 cases of coronary failure (Blumgart) were treated with " tromexan ", a derivative of dicoumarol. A dose of 600 mg. tromexan was given 8-hourly for 24 hours and further dosage so adjusted as to keep the prothrombin level at 20 to 30% of normal, usually attained by giving 600 mg. one day and 300 mg. the next. All the patients in the former group survived, but 2 in the latter died of infarction, one of these after tromexan had been stopped as all symptoms had abated. No side-effects were noted. Tromexan is stated to act more quickly than dicoumarol. [The method of estimating prothrombin is not stated.]
D. Verel

1986. **The Role of the Small Coronary Vessels in Myocardial Infarction.** (Le rôle des petites branches coronaires dans la pathogenèse de l'infarctus myocardique)
S. HIRSCH. *Acta Medica Scandinavica* [*Acta med. scand.*] 138, 449–456, Nov. 10, 1950. 11 figs., 37 refs.

In this review of his previous work the author points out that the finer branches of the coronary arteries are inaccessible to the physiologist and hitherto have been neglected by the anatomist. This important region of the coronary circulation may well be the site where a solution should be sought of the problems of infarction. Examination of portions of cardiac tissue obtained immediately after death in 20 cases, before coagulation of blood in the fine coronary vessels had taken place, has revealed the presence in cardiac tissue of fine arteriovenous anastomoses. The vascular lining in such regions consists of large, clear, epithelioid cells. In 100 rats subjected to faradic shock typical cardiac infarcts developed in the papillary muscle and intraventricular

septum some 10 to 12 days after exposure. These infarcts consisted of blockage of the fine arteriovenous connections, while the large coronary arteries remained intact. The occurrence of fine haemorrhages was indicated by deposition of haemosiderin. It is the author's thesis that angina is an " alarm reaction " and myocardial infarction a " stress disease " in Selye's terminology, and that functional cardiovascular disorder, rather than pathological change, underlies most lesions.

James D. P. Graham

1987. **Recent History of Coronary Disease**
J. N. MORRIS. *Lancet* [*Lancet*] **1**, 1–7 and 69–73, Jan. 6 and 13, 1951, 4 figs., bibliography.

In England and Wales the number of deaths from coronary heart disease doubled between 1938 and 1948. This might be due to the substitution of " coronary thrombosis " for " myocarditis " in the certificates, but the number of deaths from rupture of the heart found at coroner's inquests more than doubled during the same period. Also the number of recent infarcts found at necropsy at the London Hospital increased seven-fold between the period 1907 to 1914 and that of 1944 to 1948, the greatest increase being from 1916 to 1919, at a time when coronary occlusion was not diagnosed clinically.

The incidence of severe coronary atheroma, however, has decreased. Examination of the necropsy records at the London Hospital shows that there was less advanced atheroma, as measured by calcification of the arteries, in 1944 to 1949 compared with the years 1908 to 1913. The decrease took place mainly during the two war periods and may be ascribed to the rationing of fats.

The problem of why coronary heart disease should increase while atheroma is decreasing is discussed. It seems that while atheroma provides the basis for coronary occlusion, there are precipitating factors affecting the coagulability of the blood. It may also be that calcification of the artery represents a stage of healing, and that subintimal haemorrhages, possibly with concomitant spasm, are more likely in the earlier stages. In conjunction with the unknown precipitating factors this might account for the tendency in recent years for coronary occlusion to occur in younger age groups.

This paper establishes the fact that in spite of a decreasing incidence of calcified coronary arteries, myocardial infarction has increased in the last 40 years much more than can be accounted for by the ageing of the population. *C. W. C. Bain*

1988. **Coronary Sclerosis in Hypertension.** (Die Coronarsklerose bei Hypertonie)
W. BÄURLE. *Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie* [*Beitr. path. Anat.*] **3**, 108–124, 1950. 6 figs., 21 refs.

The coronary arteries in 8 cases of essential and 3 cases of renal hypertension were examined in detail. In contrast to hyperpiesis of arteriosclerotic origin, where stenosing sclerotic lesions tend to be localized to the proximal third of the coronary arteries, vascular changes were here demonstrated in the middle and, especially, the distal thirds. Histologically the lesions differed in no way from those observed in arteriosclerosis and frequently occupied large portions of the vessels. This feature, according to the author, predisposes to coronary incompetence and angina pectoris. *R. Salm*

DISORDERS OF CIRCULATION

1989. **Effects of Priscol on the Peripheral Circulation**
R. B. LYNN. *Lancet* [*Lancet*] **2**, 676–678, Dec. 2, 1950. 6 figs., 11 refs.

The effects of " priscol " (tolazoline; 2-benzyliminazoline) on the peripheral circulation in the limbs was studied in 40 subjects. In 6 normal adults a dose of 50 mg. given intravenously caused a marked increase in the blood flow through the hands and feet, but only a slight increase in the calf. The same dose injected into the femoral artery had a maximal effect on the blood flow through the ipsilateral foot, but only a slight increase in the contralateral foot. In 3 patients after sympathectomy the intravenous injection of 50 mg. caused no appreciable change in blood flow through the feet. In 13 patients with vasospastic disorders of the limbs (Raynaud's disease, etc.) the intravenous injection of priscol caused an immediate increase in blood flow through hands and feet. A dose of 150 mg. taken daily by mouth produced a definite clinical improvement in 3 cases of Raynaud's disease and in 5 out of 8 cases of Raynaud's phenomenon. The intravenous injection of 50 mg. of the drug in 17 patients with occlusive vascular disease was followed by increase in blood flow in the foot, but only a slight increase in the calf. Eight of these patients received 150 mg. daily by mouth with no appreciable clinical improvement. In one patient with an acute embolism of the brachial artery an injection of 40 mg. into the subclavian artery was followed by considerable improvement in the collateral circulation. It is concluded that priscol is a sympathetic blocking agent producing its greatest effect on the hands and feet. It is of value in vasospastic disorders, but is unlikely to benefit occlusive vascular disease. Its value in the treatment of acute arterial embolism and in the selection of patients for sympathectomy requires further study.

C. Bruce Perry

1990. **Therapy of Paroxysmal Pulmonary Edema by Antifoaming Agents**
A. A. LUISADA. *Circulation* [*Circulation*] **2**, 872–879, Dec., 1950. 2 figs., 19 refs.

Experiments were performed in rabbits with a series of anti-foaming agents administered by inhalation in order to counteract the effects of intravenous adrenaline, which produces fatal pulmonary oedema. Poorly volatile drugs, such as heavy alcohols and " span 85 ", had no favourable effect, and ether gave only a slight benefit. Ethyl alcohol, on the other hand, was found to possess a well-marked therapeutic action on the adrenaline-induced pulmonary oedema; after 6 minutes, 90% of the animals were still alive, the average survival time being doubled and the lungs : body weight ratio decreased from three times to double the normal. Its

effect was comparable to that of morphine. Still better results have been obtained by the combined use of morphine by injection and ethyl alcohol by inhalation, the effect of which was equivalent to that of morphine with oxygen.

The therapeutic value of ethyl alcohol was also tested in other animals (guinea-pigs, dogs) and its favourable action was confirmed.

Clinical trial is now being undertaken at the Mount Sinai Hospital, New York. The author believes that if these results are confirmed in human subjects the clinical application of ethyl alcohol by inhalation in conjunction with oxygen under pressure would seem worth while in patients with some forms of pulmonary oedema when morphine for one reason or another is contraindicated. *A. I. Suchett-Kaye*

1991. **Intra-arterial Histamine in Treatment of Claudication and Rest Pain**
W. A. MACKEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1086–1089, Nov. 11, 1950. 2 figs., 1 ref.

It is pointed out that the use of vasodilator drugs results in a generalized temporary vasodilatation, often associated with a fall in blood pressure. If the symptom demanding treatment is intermittent claudication, it may well be that in these circumstances less blood in fact may circulate in the affected limb. Sympathectomy has little effect if any on the arteries supplying the muscles, and its use in claudication is disappointing. The author therefore tried the effect of the intra-arterial injection of 2 mg. of histamine acid phosphate dissolved in 500 ml. of normal saline in 14 cases of intermittent claudication. Injection was made under pressure slowly, taking 30 to 45 minutes, into the femoral artery by percutaneous puncture. In a few seconds there was flushing in the upper thigh spreading distally to a variable degree and becoming more apparent on later occasions, and a rise in toe temperature was sometimes detected. Oscillometric records showed an immediate falling off of pulsations, but after the end of the infusion there was a marked increase. The infusions were repeated weekly for 10 weeks, and of the 14 patients, 9 showed some improvement. There were no ill effects as a result of the procedure.

[Repeated intra-arterial injection, especially if it is achieved by percutaneous puncture, must surely be a dangerous procedure, particularly in a person who already has diseased vessels.] *Peter Martin*

1992. **Pheochromocytoma and Essential Hypertensive Vascular Disease**
M. GOLDENBERG, H. ARANOW, A. A. SMITH, and M. FABER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 823–836, Dec., 1950. 3 figs., 17 refs.

This is a comprehensive paper based on the findings in 22 cases of pheochromocytoma, of which the clinical histories are given. These tumours contain adrenaline and noradrenaline in varying proportions. Continuous intravenous infusion of the former raises the systolic blood pressure, causes hyperglycaemia, augments the basal metabolic rate (B.M.R.), and produces anxiety and palpitations, whereas noradrenaline raises both the systolic and diastolic pressures, has little effect on the B.M.R., and produces the picture of classical essential hypertension, which may be mimicked in cases of pheochromocytoma.

It was found that in 7 of the 12 cases in which the pheochromocytoma was removed surgically the hypertension continued after the operation but, strangely enough, the symptoms disappeared. It would appear that although the primary stimulus had ceased, the hypertension was irreversible [compare the results of nephrectomy for hypertension]. Chemical analysis of 15 of the tumours was undertaken and it was found that where the tumour contained a large amount of adrenaline, the clinical picture was one of tachycardia, high B.M.R., and hyperglycaemia, whereas small tumours, which contained only noradrenaline, produced the pure picture of essential hypertension. The former group usually showed a strong positive reaction to the piperoxan hydrochloride test. *Paul B. Woolley*

1993. **Some Biological Properties of the Serum of Hypertensive Patients.** (О некоторых биологических особенностях сыворотки крови больных гипертонией)
A. M. NOGALLER and I. I. NEFEDOVA. Архив Патологии (*Arkh. Patol.*] **12**, No. 5, 38–43, 1950. 2 figs., 17 refs.

It is generally held that heart failure in hypertension is caused by a combination of haemodynamic disturbances, muscle hypertrophy, inadequate coronary circulation, and the toxic effect of excessive muscle metabolites. It is possible, however, that some humoral factors also participate in the process. The authors have studied the effect of blood serum from hypertensive patients on an isolated frog's heart and found that it increased the amplitude of the contractions. Whole blood was equally effective. Haemolized blood was initially active, but this activity diminished rapidly on keeping. The effect was not due to action on sympathetic nerve endings. The active principle is not a sympathicomimetic or adrenaline-like substance, and is probably not a protein. *L. Crome*

1994. **The Rice Diet in the Treatment of Hypertension. A Report to the Medical Research Council**
D. R. CAMERON, D. M. DUNLOP, R. PLATT, M. L. ROSENHEIM, and E. P. SHARPEY-SCHAFER. *Lancet* [*Lancet*] **2**, 509–513, Nov. 11, 1950. 3 figs., 28 refs.

The Kempner diet of rice, fruit, fruit juices, and sugar or syrup, with added vitamins, provides some 2,000 Calories (approximately 20 g. of protein, 5 g. of fat, and not more than 150 mg. of sodium) and a fluid intake limited to 1 litre a day. Of 41 hypertensive patients, each of whom had resting diastolic blood pressure of over 120 mm. Hg, and who were selected for treatment with the diet, several were unable to tolerate the regimen for more than a few days. Full co-operation between patient, doctor, and dietitian is essential. Relief from symptoms referable to hypertension was obtained in 25 out of 33 patients. In the majority of the 35 patients

studied for a full 6 weeks the resting blood pressure fell by an average of 55 mm. Hg systolic and 25 mm. Hg diastolic, but rose as soon as the rice diet was replaced by a low sodium diet (1 to 3 g. of sodium a day). In a few cases the heart size diminished and electrocardiographic and retinal changes improved. All the patients lost weight; when this occurred in the absence of oedema it was considered to be due to inadequate caloric or protein intake. The plasma chloride level and urinary excretion of chloride were both diminished, but the plasma sodium content usually remained unchanged. Once the patient was stabilized the urinary chloride excretion was less than 300 mg. a day and the urinary chloride estimation provided a valuable means of checking the patient's adherence to his diet. There was no correlation between fall in plasma cholesterol level and fall in blood pressure. In most cases the blood urea level fell. The authors concluded that in spite of the symptomatic relief which resulted the rice diet was impracticable as a therapeutic measure owing to the difficulty in getting patients to tolerate it for long periods. Its effect appears to be related to extreme sodium restriction rather than to low fat, protein, or caloric intake or to psychological factors. The rice diet is not without danger, particularly in patients with renal damage, where fatal uraemia or critical sodium elimination may result. *J. L. Lovibond*

See also *Abstracts of World Surgery*, 1951, **9**, 255.

BLOOD VESSELS

1995. **Dilatation of the Aorta in Arachnodactyly.** [In English]
G. A. LINDEBOOM and E. R. WESTERVELD-BRANDON. *Cardiologia* [*Cardiologia, Basel*] **17**, 217–222, 1950. 6 figs., 14 refs.

The incidence of dissecting aneurysm and aneurysmal dilatation of the aorta in reported cases of arachnodactyly is reviewed. Among 13 patients attending an ophthalmic clinic, radiological evidence of enlargement of the aorta was found in 5 cases, with clinical evidence of aortic incompetence in one. One other patient had a congenital heart lesion. *D. Verel*

1996. **Production of Experimental Cholesterol-induced Atherosclerosis in Chicks and Minimal Hypercholesterolemia and Organ Lipidosis**
J. STAMLER and L. N. KATZ. *Circulation* [*Circulation*] **2**, 705–713, Nov., 1950. 37 refs.

Feeding chicks a mash enriched with 0·25% cholesterol plus 5% cottonseed oil induced a minimal sustained hypercholesterolemia and hepatic lipidosis. This level of dietary cholesterol apparently approaches the borderline of chick tolerance for this substance. At the end of 35 weeks of the experimental diet, a high incidence of gross cholesterol-induced atherosclerosis of the aorta was present. Cholesterol-induced lesions were particularly prominent in the thoracic aorta.

Serial data on individual chick lipid levels indicated that atherosclerosis in the thoracic aorta closely paralleled the level of hypercholesterolemia. Atherogenesis did not correlate with the ratio of plasma total cholesterol to phospholipid. No other correlations could be established between biochemical and pathologic findings in either experimental or control birds.

The lipid metabolic pattern of dietary minimal hypercholesterolemia and organ lipidosis in these chicks closely simulates conditions hypothesized to be significant for atherogenesis in man. Hence the presence of atherosclerosis in these birds lends further support to the concept of the relationship of cholesterol in general, and exogenous cholesterol in particular, to the pathogenesis of human atherosclerosis.—[Authors' summary.]

1997. **Effect of Choline and Inositol on Plasma and Tissue Lipids and Atherosclerosis in the Cholesterol-fed Chick**
J. STAMLER, C. BOLENE, R. HARRIS, and L. N. KATZ. *Circulation* [*Circulation*] **2**, 714–721, Nov., 1950. 2 figs., 42 refs.

The ability of choline plus inositol to protect against cholesterol-induced atherosclerosis was studied in chicks fed 0·25%, 0·5%, and 2% cholesterol. The lipotropic factors did not lower cholesterol-induced hyperlipemia and hypercholesterolemia. They did not effect a reduction in the ratio of plasma total cholesterol to lipid phosphorus. They tended to aggravate hypercholesterolemia and hyperlipemia.

Choline and inositol exerted a partial, incomplete lipotropic effect against cholesterol-induced hepatic lipidosis and cholesterosis. They failed to affect the lipidosis and cholesterosis occurring in other organs, including the aorta. The lipotropic factors did not reduce the incidence and severity of cholesterol-induced atherosclerosis of the aorta. In all groups fed cholesterol-enriched diets supplemented with choline and inositol atherosclerosis tended to be more frequent and severe.—[Authors' summary.]

1998. **Effect of Choline and Inositol on Plasma and Tissue Lipids and on Spontaneous and Stilbestrol-induced Atherosclerosis in the Chick**
J. STAMLER, C. BOLENE, R. HARRIS, and L. N. KATZ. *Circulation* [*Circulation*] **2**, 722–725, Nov., 1950. 10 refs.

The prophylactic effect of choline and inositol against spontaneous and stilbestrol-induced atherosclerosis of the chick was studied. The lipotropic factors were found to be without effect on plasma and tissue lipid concentrations in either plain mash-fed or stilbestrol-treated birds. Choline and inositol failed to reduce either the incidence or severity of spontaneous or stilbestrol-induced atherosclerosis.—[Authors' summary.]

1999. **Experimental and Therapeutic Investigations with Certain New Hydrogenated Ergot Alkaloids in Peripheral Vascular Disorders**
A. KAPPERT and W. HADORN. *Angiology* [*Angiology*] **1**, 520–529, Dec., 1950. 2 figs., 7 refs.

See also Section Pathology, Abstract 1868; Section Dermatology, Abstract 2065.

Disorders of the Blood

2000. **Experimental Production of " L.E." Cells**
J. B. MOYER and G. S. FISHER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 1011–1015, Nov., 1950. 5 figs., 10 refs.

The authors report the production of L.E. cells by incubating active neutrophils from the buffy coat of fresh blood with altered lymphocytes in the buffy material of outdated bank blood or frozen suspensions from a case of chronic lymphoid leukemia in the presence of L.E. plasma. Wright-stained smears showed the majority of L.E. cells to come from filamented neutrophils. Phagocytosis in these cells was confirmed by supravital staining with Janus green. Complete lysis of the nuclear material ends in vacuole formation.
Ernest T. Ruston

2001. **The Effect of " Hydergin " on the Clotting Time in Haemophilia.** (Wirkung von Hydergin auf die Gerinnungszeit bei Hämophilie)
M. VODOPIVEC and N. JELAVIC. *Acta Haematologica* [*Acta haematol., Basel*] **3**, 247–254, May, 1950. 3 figs., 6 refs.

Details are given of 4 cases of typical haemophilia treated by parenteral administration of " hydergin " (an ergot derivative). In each the coagulation time was transiently prolonged over a period of about 6 hours. A similar but less intense effect was obtained by oral administration.
A. Piney

2002. **The Laboratory Diagnosis of Haemophilia**
C. MERSKEY. *Journal of Clinical Pathology* [*J. clin. Path.*] **5**, 301–320, Nov., 1950. 10 figs., 22 refs.

This is a review of the laboratory findings in 72 cases of haemophilia. In 28 cases (39%) it was impossible to trace a family history, but this may have been due to selection. The Lee and White technique of measuring coagulation time with venous blood was preferred to the capillary-blood technique of Dale and Laidlaw. However, the latter test failed to indicate a prolonged coagulation time in only 4 cases. Occasionally definitely abnormal readings were obtained with capillary blood when the venous-blood clotting time was normal. The increase of clotting time in rapidly centrifuged and recalcified plasma (Quick's test) was found to be inconstant and of little diagnostic value. The prothrombin consumption index (Merskey, *J. clin. Path.*, 1950, **3**, 130) varied in a manner roughly proportional to the coagulation time. With serum from whole clotted venous blood abnormal prothrombin consumption was found in all but 3 cases. As prothrombin consumption defects are also found in thrombocytopenic states this test is not diagnostic *per se*.

An attempt was made to assay on a rough quantitative basis the amount of normal blood required to correct the defects of haemophilic blood. Although under 1% of normal blood had a marked influence on these defects, 10% or even more was required for full correction of the clotting time and prothrombin consumption index. Three grades of haemophilia were distinguished, cases with a Lee–White coagulation time of over 15 minutes, between 10 and 15 minutes, and under 10 minutes. The gradation was reflected in the other laboratory manifestations and in the severity of the disease, but the grades were not very clearly defined and intermediate cases existed. The degree of the defect in any one case seemed to remain constant over long periods of time and was constant in any family, even over a number of generations.
Harold Caplan

2003. **Accelerator Factors in Hemophilic Blood**
W. F. ORR and M. E. GRAY. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 148–152, Oct., 1950. 31 refs.

2004. **Acute Leucosis.** (К учению об остром лейкозе)
N. A. KRAEVSKIJ and N. M. NEMENOVA. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 10, 11–19, Oct., 1950. 5 figs., 18 refs.

2005. **The Bone and Joint Lesions in Acute Leukaemia and their Response to Folic Acid Antagonists**
E. DRESNER. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 339–352, Oct., 1950. 11 figs., 33 refs.

The author describes the appearance of bone lesions in 5 cases of leukaemia occurring in children and the effect of folic acid antagonists (aminopterin and amethopterin) on them. The first 4 patients had lymphoblastic leukaemia; in the 5th patient the leukaemia was myeloblastic in type. In the former type of case the author was impressed by the effect of the folic acid antagonists in relieving the osteo-articular symptoms and reversing the bone lesions, which was demonstrated in all these patients radiologically. Small amounts of amethopterin were administered to the patient with myeloblastic leukaemia without effect.
R. Winston Evans

2006. **Folic Acid Antagonists in the Treatment of Acute and Subacute Leukemia**
W. DAMESHEK, M. H. FREEDMAN, and L. STEINBERG. *Blood* [*Blood*] **5**, 898–915, Oct., 1950. 10 figs., 13 refs.

The responses in 40 cases of acute and subacute leukaemia are described following treatment with folic acid antagonists, in particular aminopterin. Of the 40, 32 were treated for at least 7 days and remissions occurred in 10. These remissions were of a temporary nature and variable in duration. Of the 40 patients only 2 had survived. One had had an excellent remission for 25 months after the beginning of therapy; the other 3 had remissions lasting altogether 11 months, but

failed to respond to aminopterin in the third relapse. A remission of 8 weeks followed treatment with adrenocorticotrophin, but subsequent responses were poor. The best responses (clinical, haematological and bone-marrow) were seen in cases of lymphatic leukaemia, the subacute type doing better than the acute fulminating variety. In 4 cases of monocytic leukaemia there was no response.

There is a very narrow margin between the therapeutic and the toxic doses of these substances, and in fact in some cases toxic symptoms appeared to be an indication of therapeutic response. The dosage of the drug varied according to the type of folic acid antagonist; it was usually given parenterally until toxic or marked haematological reactions were produced and then the drug was discontinued. Maintenance doses were instituted for further treatment. Blood transfusions and antibiotics were given as required.

Full details of the dosage and responses to treatment are given in a table. *John F. Wilkinson*

2007. **Blood Volume in Polycythemia as Determined by P^{32} Labeled Red Blood Cells**

N. I. BERLIN, J. H. LAWRENCE, and J. GARTLAND. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 747–751, Dec., 1950. 2 figs., 26 refs.

By means of erythrocytes labelled with radioactive phosphorus (^{32}P) the total blood volume was determined in patients with polycythaemia vera, secondary polycythaemia, and relative polycythaemia. The 53 patients with polycythaemia vera fell into three groups; 32 in whom the haematocrit reading was above 55 (those in an obvious relapse), 9 in whom the reading was 50 to 54, and 10 in whom it was below 50. In the first group the total erythrocyte volume was increased, while the plasma volume tended to be low. In the second group the total erythrocyte volume was increased and the plasma volume normal, but in the third group total erythrocyte volume and plasma volume were both normal. In 6 cases of secondary polycythaemia the total erythrocyte volume was high and the plasma volume low. In 7 cases of relative polycythaemia in which the high erythrocyte count was due to low plasma volume the total erythrocyte volume was normal. It was thus found, contrary to previous reports, that the estimation of the blood volume was not of help in distinguishing between polycythaemia vera and secondary polycythaemia. In 35 patients with polycythaemia vera a direct relationship was noted between the total erythrocyte volume and the number of circulating leucocytes, supporting the view that in this condition there is a hyperplasia of the myeloid series as well as of the erythrocyte series. *C. Bruce Perry*

2008. **The Circulating Red Cell Mass in Polycythemia Vera as Determined by Red Blood Cells Tagged with the Radioactive Isotope of Iron**

P. F. HAHN, E. B. WELLS, and G. R. MENEELY. *Southern Medical Journal* [*Sth. med. J. Bgham, Ala*] **43**, 947–950, Nov., 1950. 12 refs.

A moderate degree of iron deficiency was induced in a donor-subject (Rh negative and group O) by repeated withdrawals of 500 ml. of blood. Doses of the radioactive isotope of iron were given by mouth in order to label erythrocytes in the circulating blood, and 50 ml. of this blood injected into 2 patients with polycythaemia vera. Radioactivity was assayed in 15-ml. samples subsequently withdrawn, which gave a circulating erythrocyte mass of 6,200 ml. in a man of 54 against an estimated 3,400 ml. from the body weight and venous haematocrit reading, and of 3,960 ml. in a man of 62 against an estimated 2,560 ml.

The authors also discuss treatment, advocating an initial drastic phlebotomy, to remove erythrocytes, and radiotherapy, attacking the cell at its origin, to maintain remissions thus produced. Phenylhydrazine destroys the mature erythrocyte, but liberates iron in a readily available form for the construction of new haemoglobin. *Ernest T. Ruston*

2009. **The Clinical and Haematological Features of Erythromyelosis.** (Zur Klinik und Hämatologie der Erythromyelosen)

H. LÜDIN. *Acta Haematologica* [*Acta haemat., Basel*] **4**, 321–342, Dec., 1950. 29 figs., 40 refs.

The clinical and haematological features of 4 cases of erythromyelosis (di Guglielmo's disease) are described. In each patient pathological erythrocyte precursors were found in the bone marrow with " spill-over " into the blood stream at some stage of the illness. The abnormal erythrocyte precursors were more like megaloblasts than normoblasts, but certain cytometric distinguishing features are described. In one case there was a reduction in the erythrocyte and leucocyte precursors in the peripheral blood on treatment with a folic acid antagonist, and in another case a similar reduction was observed on giving urethane.

[The close resemblance which this disease bears to other haematological conditions is obvious. If the patients had been seen for the first time in the terminal stages of their illness the following diagnoses would probably have been made: aplastic anaemia (2 cases), myelosclerosis (1 case), and acute leukaemia (1 case).] *P. C. Reynell*

2010. **Multiple Myeloma. II. Variability of Roentgen Appearance and Effect of Urethane Therapy on Skeletal Disease**

R. W. RUNDLES and R. J. REEVES. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 799–809, Nov., 1950. 4 figs., 18 refs.

The osteolytic bone lesions of multiple myeloma affect the bones that contain red marrow, the bone trabeculae adjacent to nodules of proliferating plasma cells being demineralized first. Marrow aspirated from areas of bone absorption usually contains a high proportion of plasma cells, while that obtained elsewhere may contain relatively few. Areas of plasma-cell proliferation may be isolated, multiple, or spread diffusely through the marrow, and the radiographic appearance varies according to the number and extent of areas involved.

During the active stages of the disease there may be hypercalcaemia. This subsides, and the serum alkaline-phosphatase activity rises slightly under the influence

of urethane therapy. Successive radiographic examinations, however, show little convincing evidence of bone repair during the first 3 months of the treatment, although clinical improvement is most pronounced. But after 4 to 6 months recalcification of the affected areas becomes quite definite. The sooner the treatment is instituted the better the results and prognosis. Early diagnosis is therefore most important. Examination of bone marrow aspirated from the usual sites or directly from the lesions usually supplies conclusive diagnostic evidence.

A. Orley

2011. **Guanazolo in the Therapy of Hodgkin's Disease**
B. STRAUS, S. BERSON, T. BERNSTEIN, and A. S. JACOBSON. *Blood* [*Blood*] **5**, 1059–1061, Nov., 1950. 4 refs.

Five patients with active Hodgkin's disease were treated for a period varying from 4 to 18 days with an antiguanine preparation, guanazolo (5-amino-7-hydroxy-1H-v-triazolo[d]pyrimidine), with a total dosage of 400 mg. to 800 mg. intramuscularly. No therapeutic effect was observed. The only toxic manifestations were pain and tenderness at the site of injection in 4 of the 5 cases. The effect of guanazolo on tissue cultures of an involved node was tested. No inhibition of growth was observed, thus paralleling the lack of *in vivo* effect.—[Authors' summary.]

2012. **Further Report on the Subacute Regional Lymphadenopathy with Spontaneous Cure Recently Described. Benign Lymphoreticulosis of Inoculation.** (Documentation nouvelle sur l'adénopathie régionale subaiguë et spontanément curable décrite en 1950. La lymphoréticulose bénigne d'inoculation)
P. MOLLARET, J. REILLY, R. BASTIN, and P. TOURNIER. *Presse Médicale* [*Pr. méd.*] **58**, 1353–1355, Dec. 2, 1950. 1 ref.

Continuing their studies of a hitherto undescribed type of lymphadenopathy (*Pr. méd.*, 1950, **58**, 282; *Bull. Soc. méd. Hôp. Paris*, 1950, **66**, 424), the authors report their findings in 42 cases, of which 21 were due to scratching and biting by cats, while the other patients developed the condition after a prick with a thorn or a splinter. The result of these wounds was an intensive reaction in the lymph nodes nearest to the injury. The authors suggest that the condition be termed " benign lymphoreticulosis ". In histological preparations they demonstrated a reticular proliferation associated with small abscesses. They suspect a virus to be the infective agent. On immunological examination of the pus they have distinguished 6 antigens producing an allergic reaction on intradermal injection in the affected patients, while in control patients, affected by an adenopathy of different origin, the reaction was completely negative. Serological investigation of 13 patients with a complement-fixation test based on that used for lymphogranuloma venereum showed a deviation of complement in 11 cases. The authors are of the opinion that the agent of this benign lymphadenopathy belongs to the same virus family as those of lymphogranuloma venereum and psittacosis. They were, however, unable to identify the virus either by culture or by inoculation. *Franz Heimann*

ANAEMIA

2013. **The Intestinal Content in Pernicious Anemia of Factors for the Growth of *Streptococcus faecalis* and *Lactobacillus leishmannii***
R. H. GIRDWOOD. *Blood* [*Blood*] **5**, 1009–1016, Nov., 1950. 30 refs.

In 3 patients with untreated pernicious anaemia and 2 controls the intestinal contents were aspirated with a sterile Cantor tube at various levels between the stomach and caecum, and the amounts of pteroyl glutamic acid and vitamin B_{12} at each level were estimated by microbiological assay. Very small concentrations only of both substances were detected in all patients and there was no progressive decrease in concentration of the factors in the lower levels of the intestine. The faecal content of both factors was relatively high in all patients. These results do not suggest that the bacteria of the small intestine play any very important part in the formation or destruction of pteroyl glutamic acid or vitamin B_{12} either in patients with untreated pernicious anaemia or in normal subjects. [Although the amounts of both substances recovered from the small intestine were very small, patients were fasting throughout the period of the investigations, which lasted some 36 hours.]

P. C. Reynell

2014. **Erythroblastosis Fetalis. IV. Further Observations on Kernicterus**
V. C. VAUGHAN, F. H. ALLEN, and L. K. DIAMOND. *Pediatrics* [*Pediatrics*] **6**, 706–716, Nov., 1950. 21 refs.

The incidence of kernicterus was studied in all the infants with erythroblastosis foetalis born alive at the Boston Lying-in Hospital from 1945 to 1948, or admitted to the Children's Hospital, Boston, in 1947 to 1948. The frequency of kernicterus in the infants born alive was 12% and 5% in those infants surviving the first week of life. The greater the intensity of maternal sensitization the more likely is kernicterus to develop. The authors consider kernicterus to be a disease of neonatal life, more likely to occur when the period of gestation has been less than 38 weeks, so that immaturity more or less cancels any gain obtained by induction of labour. There would appear to be a familial tendency to kernicterus, as with a past history of a previously affected infant the chances increase of this complication reappearing in a subsequent live-born Rh-positive infant.

W. G. Wyllie

2015. **Studies of the Influence of Sex of Donor on the Survival of Erythroblastotic Infants Treated by Exchange Transfusion**
M. S. SACKS, C. L. SPURLING, I. D. J. BROSS, and E. F. JAHN. *Pediatrics* [*Pediatrics*] **6**, 772–777, Nov., 1950. 3 refs.

In view of suggestions that transfusion of female blood rather than male improved the chances of survival of infants with erythroblastosis, the authors present an analysis of 55 cases, of which 23 received blood from female donors and 32 from male donors. The over-all mortality was 17·6%, and no advantage was

observed from the use of female as opposed to male blood in exchange transfusions, even in cases of a severe type. *W. G. Wyllie*

2016. **March Hemoglobinuria in a Woman**
D. R. GILLIGAN and M. D. ALTSCHULE. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 944–948, Dec. 14, 1950. 2 figs., 32 refs.

The only previously recorded instance of the occurrence of march haemoglobinuria in a woman was described in 1943 by Vogt *et al.* (*Dtsch. Arch. klin. Med.*, **191**, 488). Another case is here reported, in a woman aged 30 years who complained of passing red urine after walking half a mile (0·8 km.) in 10 minutes. Physical examination revealed no abnormality, but the complexion was somewhat sallow. The erythrocyte count was 3,790,000 per c. mm. and the haemoglobin level 12·4 g. per 100 ml. Probably the slight degree of anaemia was due to a dietary deficiency, for it disappeared after ferrous sulphate therapy.

During the course of the investigation the patient walked distances ranging from 1 to 15 miles (1·6 to 24 km.). Cramps occurred while the patient walked 15 miles and the cramps persisted for a brief period after the walk had ended. Spectrophotometric studies revealed that exertion had resulted in the release of haemoglobin into the plasma and urine. Unless the walk was unusually prolonged the degree of haemolysis showed an increase in direct proportion to the distance walked. After walks of 1 to 3 miles the plasma haemoglobin concentration amounted to 32 to 64 mg. per 100 ml. Obvious haemoglobinuria was observed when the amount of haemoglobin in the plasma reached the level of 50 mg. per 100 ml. In these circumstances the nitric acid test for proteinuria became strongly positive, and the haemoglobinuria persisted for 3 to 4 hours. The urine contained from 5 to 20% of the haemoglobin released into the plasma. Changes in posture failed to affect the rate of haemoglobin precipitation. No evidence was found that the patient's disability was due to the effect of cold, syphilis, favism, or acute haemolytic anaemia; nor was the condition associated with either myoglobinuria or paroxysmal nocturnal haemoglobinuria. *A. Garland*

2017. **The Anemia of Infection. XIV. Response to Massive Doses of Intravenously Administered Saccharated Oxide of Iron**
W. J. KUHNS, C. J. GUBLER, G. E. CARTWRIGHT, and M. M. WINTROBE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1505–1513, Nov., 1950. 11 figs., 20 refs.

Evidence of the effect of intravenous iron in the hypochromic anaemia of infection, particularly that associated with rheumatoid arthritis, is conflicting. The present authors have recently made an intensive study of 14 cases. They conclude that despite the large doses given and a rise in serum iron level immediately following treatment, in no instance where the associated illness persisted following therapy was the hypoferremia permanently corrected. In no case was there a reticulocytosis or haemoglobin rise comparable to that found in patients with a straightforward iron deficiency. In 3 cases urinary iron was estimated, and in one the iron in a purulent exudate: loss of iron by these routes was not significant. In 2 patients who subsequently died analysis of viscera showed that an amount corresponding to 46 to 88% of the administered iron was recoverable in the liver and spleen. The reason for this diversion of iron to the tissues remains obscure. The authors suggest that since the satisfactory response obtained by Sinclair and Duthie (*Lancet.*, 1949, **2**, 646; *Brit. med. J.*, 1950, **2**, 1257) was associated with a fall in erythrocyte sedimentation rate there was possibly an equal improvement in the clinical condition of the patient, and therefore in the anaemia, which was not due to iron therapy. *Janet Vaughan*

2018. **The Occurrence in a Family of Sicilian Ancestry of the Traits for both Sickling and Thalassemia**
W. N. POWELL, J. G. RODARTE, and J. V. NEEL. *Blood* [*Blood*] **5**, 887–897, Oct., 1950. 3 figs., 36 refs.

Examination of a Sicilian family over three generations showed the presence of the sickling phenomenon in the father and a gene for thalassaemia in the mother. A 38-year-old son was found to have a chronic haemolytic anaemia of the sickle-cell type as well as evidence of thalassaemia. His 2 sons were also found to have thalassaemia minor, while his brother and 2 nephews showed the sickling trait. Three possible hypotheses are discussed to account for the severity of the anaemia in the 38-year-old patient; the authors suggest that many of the reported cases of sickle-cell disease in Caucasians may actually involve a genetic situation comparable to the one reported here. *John F. Wilkinson*

2019. **Mediterranean Anemia in Children of Non-Mediterranean Ancestry**
H. K. SILVER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 767–778, Nov., 1950.

The anaemia described by Cooley and Lee in 1925 occurred in natives of the Mediterranean area and was characterized by progressive pallor, splenomegaly, and a mongoloid facies. The disease had a familial incidence, the anaemia was microcytic and hypochromic, target cells were present, the erythrocytes showed an increased resistance to hypotonic salt solutions, and characteristic bone changes were found in the radiograph.

Since these cases were described the syndrome has been recognized in patients of non-Mediterranean stock, and reports of cases showing minor manifestations of the syndrome have appeared. In this paper the clinical features in 10 patients from 4 non-Mediterranean families are recorded. In most of the patients the disease was of the mild type, and radiological changes in the bones were present in only one case. The diagnosis was established by haematological examination, anaemia of the hypochromic microcytic type, target cells, and decreased erythrocyte fragility being found.

Symptomatic treatment was given with blood transfusions and administration of iron by mouth.
R. M. Todd

Respiratory Disorders

2020. **Observations on Changes Taking Place in the Upper Respiratory Tract of Patients under ACTH and Cortisone Therapy**
J. E. BORDLEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 415–424, Nov., 1950. 4 figs., 3 refs.

Changes have been noted in the tissues of the upper air passages under adrenal cortical stimulation by ACTH and following the administration of cortisone. During exhibition of ACTH the nasal mucous membranes lose their swelling, develop a slate-pink colour and are covered with a thin layer of clear mucus. Polyps lose their translucence, become pink and begin to shrink, in many cases disappearing completely. Such changes seem to be correlated with the initial eosinopenia developing under ACTH therapy. Changes have also been observed in the nasopharyngeal lymphoid tissue. It becomes clearly outlined from its surrounding structures, developing an orange-pink colour. Discharge around it clears up and the crypts become more prominent. Microscopic studies show no demonstrable change in such lymphoid tissue or in the nasal polyps.

The changes in the nose and nasopharynx regress after discontinuing therapy. Within a few days the nasal mucosa loses its dusky appearance, and the lymphoid tissue returns to its former state. Nasal polyps return in from 2 weeks to 2 months.

Cortisone therapy has very much the same effect on the tissue of the respiratory tract, except that no marked colour change was noted in the nasal mucosa or in the nasopharyngeal lymphoid tissue in the patients under such treatment. Nasal sprays of cortisone have resulted in a slow but definite regression of nasal polyps.—[Author's summary.]

2021. **Tropical Pulmonary Eosinophilia.**
J. D. BALL. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy Soc. trop. Med. Hyg.*] **44**, 237–258, Dec., 1950. 8 figs., 49 refs.

Many known pathogens, including helminths, amoebae, fungi, brucellae, and allergens, cause pulmonary lesions associated with eosinophilia, but are not confined to the tropics. Similarly many tropical diseases cause eosinophilia not necessarily associated with pulmonary lesions. The author therefore makes a plea for the use of both prefixes, "tropical" and "pulmonary", in describing the syndrome of eosinophilia of unknown aetiology associated with pulmonary lesions and occurring almost exclusively in the tropics. This syndrome was first fully described by Frimodt-Möller and Barton in 1940 in South India and was redescribed in 1943 in Bombay by Weingarten, who discovered the efficacy of neoarsphenamine in its treatment.

Of the thousand or so cases reported so far 95% were from India, the others from the Far East as far north as Korea, Northern Australia, West and Central Africa, the West Indies, and S. America. One hundred consecutive cases from the Vellore Christian Medical College Hospital are analysed, 51 being in children under 15 years of age. Wet weather seems to aggravate the symptoms, which are present from 2 to 9 months before advice is sought. These are cough, mostly nocturnal and often in paroxysms, wheezing, and dyspnoea, all coming in "attacks" which recur at varying intervals. Occasionally there is blood-streaked sputum and retrosternal pain, and about half the cases have a febrile stage. Lung signs are creaking medium or coarse basal crepitations and scattered rhonchi. Children tend to show lymph-node enlargement. Leucocytosis is almost entirely due to the eosinophils, which may exceed 50,000 but average 6,000 per c.mm. *X*-ray examination of lungs shows increased striation, miliary mottling, and hilar lymph-node enlargement. Neither mites nor helminths can be incriminated. Oxophenarsine hydrochloride appears the best and safest remedy for adults, and acetarsol for children without veins suitable for injection. Neoarsphenamine is liable to cause encephalopathy. Arsenotherapy cures about 50%, gives partial relief in most, but fails to cure a small minority of cases.

(In the discussion, Treu stressed the radiological and blood-picture remissions which often made diagnosis difficult, but he had never seen a failure with arsenic therapy. Oswald mentioned the prolonged pulmonary eosinophilia of temperate climates, sometimes associated with asthma, and stated that periarteritis nodosa sometimes shows pulmonary infiltration, so that a variety of diseases appeared to merge, or to be phases of a single condition. Viswanathan reported the results of injection of whole blood from cases into rabbits and guinea-pigs which at necropsy showed pulmonary changes and eosinophilia. Wilson reported a few cases from East Africa.) *Clement Chesterman*

2022. **Bronchopulmonary Hypogenesis. Diagnosis in the Living**
I. MESCHAN and J. D. CALHOUN. *Southern Medical Journal* [*Sth. med. J. Bgham, Ala*] **43**, 1038–1042, Dec., 1950. 4 figs., 11 refs.

A 38-year-old man was found, as the result of routine radiography, to have a condition diagnosed as hypogenesis of the right lung. The radiograph showed gross displacement of the heart and the trachea to the right side, with loops of intestine occupying a large part of the right hemithorax. A barium-enema examination showed that the ascending colon, caecum, appendix, and terminal ileum were contained within the thorax. Bronchograms showed filling of the right upper-lobe bronchus and its branches; two branches of the right lower-lobe bronchus were identified, but the greater part appeared to end in a blind sac 3 cm. beyond the carina. Bronchoscopy showed the orifice of the right upper-lobe bronchus, but the right stem bronchus appeared to end blindly about 3 cm. below its origin, and no segmental orifices were identified.

The authors consider that the case falls into the third category of the classification of bronchopulmonary hypogenesis by Schneider (*Amer. J. med. Sci.*, 1948, **215**, 665), namely, hypogenesis of pulmonary tissue with a fully developed bronchus ending in a fleshy mass of alveolar tissue, and that there was also a congenital abnormality of the right hemidiaphragm permitting herniation of abdominal contents into the thorax.

[It will be noted that bronchographically two branches of the right lower-lobe bronchus were identified, whereas bronchoscopically no branch bronchial openings were observed beyond the upper-lobe orifice. This discrepancy leaves reasonable doubt about the validity of the evidence on which a diagnosis of hypogenesis of the bronchopulmonary tree is made rather than atelectasis.]

J. G. Scadding

2023. **Pulmonary Sclerosis.** [In English]

O. JERVELL. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 430–436, Nov. 10, 1950. 2 figs., 24 refs.

From the Medical Department of the Louisenberg Hospital, Oslo, the author reports 4 cases of chronic cor pulmonale, with evidence of significant pulmonary arteriosclerosis in 2. The role of pulmonary hypertension, infection, and age are discussed in relation to the development of pulmonary arteriosclerosis. The difficulty of distinguishing the primary or idiopathic form from the secondary is emphasized, and the author concludes that this distinction is of little value. The observation of pulmonary oedema in all these cases is interesting, but is not adequately explained. [It should be noted that the evidence for pulmonary hypertension was all indirect and that catheterization was not performed.]

R. N. Johnston

2024. **Pulmonary Dystonia.** (Die " pulmonale Dystonie ")

M. KIBLER and A. SCHIMMEL. *Münchener Medizinische Wochenschrift* [*Munch. med. Wschr.*] **92**, 1361–1366, Nov. 24, 1950. 10 refs.

The syndrome of " pulmonary dystonia ", although common, is frequently unrecognized. The most important diagnostic feature is the contrast between the severity of the dyspnoea and the scarcity of abnormal physical signs. More than 100 patients have been observed and in all it has been possible to demonstrate zones of hyperalgesia over certain areas of the upper chest wall and the shoulders. Injection of procaine, sodium bicarbonate solution, or air subcutaneously in these areas, followed by massage, has been found an effective treatment.

[The syndrome is more generally considered to be a " respiratory neurosis ".]

J. R. Bignall

2025. **Suppurative Pneumonia**

H. NICHOLSON. *Lancet* [*Lancet*] **2**, 549–554 and 605–611, Nov. 18 and 25, 1950. 40 figs., bibliography.

These papers were delivered as the Goulstonian Lectures of 1950 at the Royal College of Physicians and are based on the author's experience at a military hospital in the Middle East during the war of 1939–45 and on the records of the Brompton Hospital. After defining suppurative pneumonia as " an inflammatory consolidation of the lung which proceeds in whole or in part to suppuration ", he discusses briefly the suppurative pneumonias due to specific organisms and to bronchogenic carcinoma; cases in the former group almost invariably resolve completely. Then follows a more detailed account of non-specific suppurative pneumonia in its various degrees of severity, the mildest form being benign aspiration pneumonia, the severest lung abscess. These are due to inhalation of infected material. The division of cases into foetid and non-foetid is not possible with any degree of accuracy; foetor comes and goes and is usually present in all at some time; its presence makes no difference to treatment and prognosis.

A number of cases become chronic and these form the basis of the rest of the paper. Cases of chronic non-specific suppurative pneumonia make up one-third of the non-tuberculous admissions to the Brompton Hospital, mostly being in males in the 5th decade. Of the 28 cases found suitable for discussion the cause was found in 19: in 7 it was dental sepsis; in 2 dental extraction; in 2 operation under general anaesthesia; in 5 chronic bronchitis; in 1 prolonged sea-bathing; in 1 the giving of thiopentone for psychiatric investigation; in 1 malnutrition. Twelve patients had been ill for more than 12 months, with some periods of remission.

Of 25 cases seen in the Middle East, 5 with an acute onset developed a cavity in under 3 weeks, while 10 did not; 7 were of gradual onset with a cough and gradually increasing fever. In all cases there was an initial febrile period which did not persist for more than a few weeks. The amount of purulent sputum was usually 2 to 7 oz. (57 to 200 ml.) daily, but in one case it was 2 pints (1,140 ml.) and in another there was only a trace of muco-purulent sputum for the first few months. Most patients had slight, and 4 had repeated and severe, haemoptyses, the largest loss being 1 pint. Almost all had clubbing of the fingers. The leucocyte count was usually 10,000 to 12,000 per c.mm., the differential count being normal.

Radiological examination showed that in the military hospital series early cavitation occurred most frequently in the posterior and axillary portions of the posterolateral segments of the upper lobes. Consolidation was usually, but not always, segmental; spread might occur directly into surrounding lung or by aspiration into distant parts. Empyema occurred in 2 cases, both healing after drainage. Pathological examination was performed in 12 cases of the first group and 13 of the second. The cavities were lined with granulation tissue, with more or less fibrosis, or sometimes with columnar or squamous epithelium, and were sometimes filled with fluid which was organizing. Occasionally there were groups of fat-containing cells filling the alveolar spaces, resembling lipoid pneumonia. Bronchi were distorted and dilated and in some instances distended and forming the walls of cavities; at some points in the bronchial wall there was complete necrosis, at others inflammatory infiltration, and at others fibrosis.

Conservative treatment resulted in only 3 of the civilian and 2 of the military patients becoming symptom-free with slight radiological change; 7 and 2 patients

respectively were improved but had severe fibrosis, while 4 and 9 were left with progressive disease. Twelve civilian patients were treated surgically, 10 by lobectomy and 2 by pneumonectomy, all but 2 with a satisfactory result. Nine military patients underwent lobectomy and one pneumonectomy; 4 deaths occurred, but in the other cases the results were satisfactory.

The author recommends that the patient should be treated with postural drainage, penicillin in doses of one million units daily, and a one-week course of a sulphonamide in the usual dosage. The patient will improve quickly, but after 2 weeks the organisms in the sputum may have become penicillin-resistant, in which case one of the other antibiotics may be tried. In the majority it is possible to achieve by these measures a state in which there is little purulent sputum, a feeling of well-being, and radiographic evidence of fibrosis. This must be regarded as a satisfactory result in some patients, many of whom will have further episodes of pulmonary infection. Where practicable pulmonary resection is the measure most likely to restore the patient to health and to stop the progression of the disease.

[These papers contain an excellent historical survey of the subject and are an important contribution to the literature. They should be read by all interested in pulmonary disease.] *A. Gordon Beckett*

2026. **Effects of Adrenocorticotropic Hormone in Pneumonia: Clinical, Bacteriological and Serological Studies**

E. H. Kass, S. H. Ingbar, and M. Finland. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 1081–1098, Nov., 1950. 5 figs., 10 refs.

Three patients with pneumococcal and one with viral pneumonia were treated with varying amounts of adrenocorticotrophin (ACTH); in another patient with viral pneumonia the administration of ACTH seems to have coincided with the beginning of natural recovery. These studies, made by the authors at the Boston City General Hospital, do not suggest any superiority of ACTH over the sulphonamides or penicillin in the treatment of pneumonia.

The details given suggest that full clinical control of the disease is obtained more slowly, an impression supported by the persistence of irregular fever for 8 to 12 days in 2 of the 3 pneumococcal cases and by a severe recrudescence in the third, in which empyema also developed after 4 weeks, by the absence of any demonstrable effect of ACTH on the pneumococci, and by the persistence of rusty sputum or bacteriaemia despite clinical improvement. On the other hand, ACTH seems to have induced remarkable crises on the 3rd day in 2 patients with pneumococcal pneumonia, and a sharp lysis on the 4th day in the other. Symptomatic relief, as shown by disappearance of pain, lessening of toxaemia and headache, and general subjective improvement, was notable. The appearance of antipneumococcal antibodies and cold agglutinins was neither delayed nor accelerated. Two patients developed glycosuria and 2 facial oedema. There was some evidence to support an antipyretic action of ACTH. *Maxwell Telling*

2027. **Pulmonary Adenomatosis. A Report of Four Cases**

J. C. King and D. S. Carroll. *Radiology* [*Radiology*] **55**, 669–680, Nov., 1950. 9 figs., 18 refs.

In benign pulmonary adenomatosis firm nodules, varying in size, are scattered throughout both lungs. Grossly, these nodules resemble areas of pneumonic consolidation and on the cut lung surface they look like foci of gray hepatization in pneumonia. A mucoid material can be expressed from the involved areas. The smaller bronchi are filled with frothy, thin, mucoid material, and areas of congestion and oedema are present throughout the lungs. In the terminal stages there is usually a considerable pneumonic consolidation superimposed upon the adenomatosis. The pleura is usually not involved, but there may be fibrinous or fibrous pleural adhesions. In typical cases there are neither regional nor distal metastases.

Microscopically, the process is much more extensive than the macroscopical appearance suggests. The alveoli are lined with cuboid and columnar epithelium which in places forms intra-alveolar papillae. The alveolar epithelium is usually uniform in appearance and is non-ciliated. There are few or no mitotic figures. The walls of the alveoli are oedematous but not infiltrated, and there is a varying degree of interstitial fibrosis.

The authors go on to discuss the clinical features and radiographic appearances of the condition and report 4 personal cases, all of which were fatal.

A. Orley

2028. **Pulmonary Adenomatosis: Further Roentgen Observations**

L. W. Paul and J. H. Juhl. *Radiology* [*Radiology*] **55**, 681–691, Nov., 1950. 13 figs., 8 refs.

Four cases of pulmonary adenomatosis are reported and the controversial points concerning this disease are discussed. The pathological picture varies. In its simplest form it resembles a benign growth. The significant clinical findings are dyspnoea and cough with a large amount of watery sputum. Death results from interference with the normal functions of the lungs and from superadded infection. In other cases the basic histological picture is the same, but there are also areas showing frank carcinomatous changes and there may also be distant metastases.

The most common radiographic findings are single or multiple areas of homogeneous density resembling pneumonic consolidation. There is no atelectasis and no involvement of the mediastinal nodes or of the pleura. The disease is slowly progressive, gradually involving nearly the whole of the pulmonary parenchyma. Less frequently the lungs show nodular shadows resembling carcinomatous metastases. Cytological examination of the sputum may give a clue to the diagnosis in some cases.

So far treatment, including lobectomy and pneumonectomy, has been of no avail, probably on account of the multicentric, widespread origin of the disease.

A. Orley

See also Section Pathology, Abstract 1895.

Digestive Disorders

2029. **Amino Acid Excretion in Patients with Gastro-intestinal Disease during Ingestion of Various Protein Supplements**

A. L. SHEFFNER, J. B. KIRSNER, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **16**, 757–763, Dec., 1950. 15 refs.

The " wastage " of amino-acids by excretion in the urine and faeces is greater when protein hydrolysates are administered orally than when more natural protein foods are given. These were the authors' findings in balance experiments in one normal subject, 2 patients with gastric ulcer, and 2 with ulcerative colitis. A meat-and-egg diet appeared to be the most efficient source of protein, dried and evaporated milk being possibly slightly inferior. The faecal excretion of amino-acids was highest in patients with gastric ulcer and ulcerative colitis who were taking protein hydrolysate by mouth. It is suggested that the complete evaluation of protein foods should include estimation of amino-acid excretion.

J. Naish

2030. **Esophageal Dysphagia, associated with Gall-bladder Disease**

M. FELDMAN. *Review of Gastroenterology* [*Rev. Gastro-ent.*] **17**, 1044–1047, Nov., 1950. 2 figs.

Two cases are reported in which an oesophageal abnormality was associated with gall-stones. The author believes that in many cases an oesophageal abnormality is not demonstrated by an ordinary barium-swallow examination. He recommends radiologists to make more use of large cotton pledgets soaked in barium sulphate.

In the first case a woman, aged 49, with a long history of " upper abdominal pain and other gastrointestinal symptoms referable to the gall-bladder " complained of difficulty in swallowing for 9 months. The difficulty was greater with solid foods. A pledget of cotton impregnated with barium became " wedged in the mid-oesophagus and remained there for over 30 minutes ". Oesophagoscopy showed no pathology but cured the symptoms and a second *x*-ray examination was normal. " It was obviously concluded that the dysphagia was due to reflex spasm due to the gall bladder condition." [The logic of this conclusion is obscure.]

In the second case, a male alcoholic aged 50 complained of intermittent periods of dysphagia for solids for 4 years. Radiology showed " evidence of oesophageal spasm and stricture at the cardia end". Oesophagoscopy confirmed the stricture, but the patient complained that his symptoms were much worse after dilatation. Following this he apparently had about 6 fairly good months with only mild and intermittent symptoms. This period came to a close with an emergency operation for acute cholecystitis. After the operation his oesophageal symptoms subsided dramatically, but he refused another *x*-ray examination. [The duration of the follow-up and alleged cure is not stated. There are several ways in which gall-bladder lesions may cause oesophageal symptoms. In dogs stimulation of the gall-bladder and other intra-abdominal viscera has been reported to cause reflex oesophageal shortening, but there is no evidence that this mechanism exists in man.]

Denys Jennings

2031. **An Experimental Study of Motor Function of the Oesophagus.** (La motricité de l'oesophage. Étude expérimentale)

Y. DUWEZ. *Acta Gastro-enterologica Belgica* [*Acta gastro-ent. belg.*] **13**, 961–968, Sept.–Oct., 1950. 5 figs., 28 refs.

The treatment of surgical affections of the oesophagus and cardia has recently been brought to notice as a result of the brilliant techniques of resection and amputation devised by thoracic surgeons. Unfortunately, however, treatment of the functional disorders has not progressed equally, and this is mainly due to confusion regarding their aetiology and to the contradictory opinions about the physiology and pathology of the structures concerned.

The author of this paper deals with one of these functional troubles, cardiospasm, and, after recapitulating the existing theories of its origin, goes on to give details of experiments carried out to investigate the physiological aspects of the theories.

Theory of Spasm.—The cardia is a sphincter subjected to vagal and sympathetic control, the vagus relaxing and the sympathetic contracting it. Destruction of the vagus produces cardiospasm as the sympathetic alone is acting, but cardiospasm disappears if this action ceases. Thus cardiospasm is due to a lesion in the para-sympathetic, but it is the integrity of the sympathetic which maintains it. This has been supported both experimentally and at necropsy. Lendrum, however, denies the existence of any morphological sphincter whatever at the level of the cardia in man, cat, or dog. The author is convinced of the absolute separation of the ortho- and para-sympathetic systems, but Carlson, Boyd, and Pearcy, by peripheral stimulation of the vagus in the dog, produced hypertonus of the cardia if it was hypotonic and vice versa.

Theory of Achalasia.—There is a co-ordination defect in deglutition between the oesophageal movements and the opening of the cardia, due to a fault in the impulse conduction. Numerous morbid anatomists support this, and a considerable reduction in the number of meta-sympathetic neurones was always observed by Lendrum. Etzel suggested a vitamin deficiency to explain this alteration in Auerbach's plexus.

Theory of Dynamic Insufficiency of the Oesophageal Walls.—Zenker, Rosenheim, and others maintain that the lesion is in the oesophageal wall, and consequently there is insufficient peristalsis. The cardia is simply closed, this being its position of rest.

Theory of Phrenospasm.—The cardia is closed by

spasmodic contraction of the layers of the diaphragm (Bassler and Chevalier Jackson).

Theory of Extrinsic Mechanical Obstruction.—Compression can be produced by an insufficient hepatic tunnel, by torsion of an overloaded oesophagus, or by fibrosis of the peri-oesophageal connective tissue (Mosher).

By means of an ingenious oesophageal sound which was swallowed by a trained sheep-dog the motor functions of the oesophagus were investigated.

Under normal conditions the oesophagus showed an average of 24 phases of activity per hour, each phase consisting of 3 or 4 unequal contractile waves; no antiperistalsis was ever observed, all waves originating in the oesophagus and travelling towards the cardia, where the waves, though retaining the same rhythm, gained amplitude.

Following the subcutaneous injection of histamine, acetylcholine, and insulin there was always an increased motor activity of the oesophagus. With histamine and acetylcholine no antiperistalsis was observed; with insulin, however, secondary centres of wave propagation were noticed, originating in the cardia and either moving towards the oesophagus or remaining localized.

Since doubt had existed regarding the action of adrenaline, the author, giving 0·2 mg. intravenously, showed that there always followed a reduction in motor activity of the oesophagus, no antiperistalsis being observed.

The results are tabulated as follows:

	Rhythm (Average and Extreme Figures)	No. of Contractile Waves in Each Phase of Activity.	Antiperistalsis
Normal ..	24 (15 and 28) per hr.	3 or 4	−ve
Histamine ..	41 (36 „ 47) „	4 to 6	−ve
Acetylcholine	42 (35 „ 48) „	4 or 5	−ve
Hypoglycaemia (Insulin) ..	70 (52 „ 90) „	6 to 12	+ve
Adrenaline ..	3 (4 „ 12) „	1 or 2	−ve

M. Beaton

STOMACH

2032. **Benign Disease of the Antral Portion of the Stomach. Benign Gastric Polyps and their Relation to Carcinoma of the Stomach**

R. V. Edwards and C. H. Brown. *Gastroenterology* [*Gastroenterology*] **16**, 531–538, Nov., 1950. 2 figs., 9 refs.

Opinions differ on the risk of malignant change occurring in polyps of the stomach. From a study of 32 cases, constituting 2·8% of all gastric neoplasms seen in 10 years at the Cleveland Clinic, the authors conclude that malignant change does occur. Benign adenomatous polyps were found in 17 of the 32 cases, and carcinomatous change arising in adenomatous polyps in 5, while in the other 10 the polyps were of connective-tissue origin. Symptomatology was indefinite, with epigastric discomfort the most frequent complaint; pain suggesting ulceration sometimes occurred and anaemia, pyloric obstruction, and haematemesis are also described. In diagnosis the test meal was not helpful (achlorhydria was common), but radiological and gastroscopic investigation, often having to be repeated, revealed or suggested the nature of the lesion in most cases.

A case is quoted in which a carcinoma developed 8 years after a benign polyp was excised. Thus while simple removal is advisable in all cases because of the risk of malignancy, more radical treatment may be required if the risk is to be eliminated entirely. *K. Gurling*

2033. **Hormone Studies in Peptic Ulcer. Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone**

D. J. Sandweiss, H. C. Saltzstein, S. R. Scheinberg, and A. Parks. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1436–1442, Dec. 23, 1950. 26 refs.

The authors present a preliminary report on the effect of adrenocorticotrophic hormone (ACTH) and cortisone in the treatment of peptic ulcer. The effect of this hormone was tested on 12 dogs in which experimental ulcers had been produced by the Mann–Williamson operative technique and on 11 control animals: 10 mg. of cortisone acetate was given subcutaneously or intramuscularly twice daily throughout the life of the animal, the treatment being started 13 to 30 days after operation. The dosage of ACTH used was 5 to 7·5 mg. by either route twice daily and was started 8 to 35 days after the operation.

It was found that the dogs treated with cortisone lived, on an average, twice as long as the control animals. Those treated with ACTH lived longer than the controls, but not so long as the cortisone-treated animals. The treated animals as a group were in a good state of nutrition and vigour as compared with the untreated ones. Similar results were obtained in Mann–Williamson dogs treated with an extract made from pregnant mare's urine (" wroanthelone ", " kutrol ") which indicates that this effect of cortisone and ACTH is not specific.

The urinary excretion of 11-oxycorticosteroids and 17-ketosteroids was studied in 31 normal subjects and 14 patients suffering from duodenal ulcer. In twelve of the latter steroid excretion was studied during an attack and repeated during a remission of symptoms. Those with active duodenal ulcer showed a statistically significant diminution of urinary excretion of 11-oxycorticosteroids as compared with normal subjects, and as compared with their excretion during a symptom-free period. This finding indicates that there is diminished adrenal activity during the active phase in duodenal ulcer.

Treatment of active duodenal ulcer with these hormones was carried out on 4 patients, 2 of whom received 1,300 mg. of cortisone over a period of 11 days. One failed to respond, but the other became symptom-free with marked feelings of well-being, which continued up to 9 months after treatment. In both cases there was a decided response to the cortisone as shown by increased steroid excretion and fall in the eosinophil count.

In treating 2 patients with ACTH the first received

100 mg. per day (33·3 mg. 8-hourly by intramuscular injection). On the 4th day of treatment the symptoms became worse and by the 9th day had reached the stage of impending perforation; hormone treatment was then stopped. The second patient was given a dosage of 15 mg. 6-hourly for 4 days, 20 mg. 4-hourly for 4 days, 25 mg. 4-hourly for 2 days, and finally 33·3 mg. 8-hourly for 6 days. Symptoms abated on the 5th day and after the 12th day the patient became symptom-free. A few days after discharge from hospital the symptoms recurred. The response to the administration of ACTH was marked by an increased urinary excretion of steroids and a lowering of the eosinophil count.

From the material available the authors are of the opinion that, in peptic ulcer, cortisone by injection or pregnant mare's urine given orally might be of value before resorting to surgical measures, but that pituitary adrenocorticotrophic hormone should be used guardedly, if at all. *M. Beaton*

2034. **The Synthetic Ion-exchange Resins in the Treatment of Gastritis and Peptic Ulcer.** (Le resine sintetiche scambiatrici di ioni nel trattamento delle gastriti e dell'ulcera gastro-duodenale)
S. LENTINI, U. GIANGRANDI, and G. PAMPANELLI. *Minerva Medica* [*Minerva med., Torino*] **2**, 1024–1032, Nov. 17, 1950. 6 figs., bibliography.

The disadvantages of drug therapy, especially with alkalies, in the treatment of gastro-duodenal disease are well known, and the use of so-called " ion-exchange " resins may well prove to have abolished these dangers. The condensation of diamine with phenol and formaldehyde results in the production of a synthetic resin in the form of a finely divided, insoluble, yellow powder, capable of combining with acid in the following manner:

$$R\text{–}NH_2 + HCl = R\text{–}NH_3Cl$$

Thus an ionic equilibrium is established which is disturbed only by passage through the intestine, with liberation once more of the resin:

$$R\text{–}NH_3Cl + NaOH = R\text{–}NH_2 + NaCl + H_2O$$

The compound is completely inert, and passes through the intestine without producing any disturbance of peristalsis or any known toxic effect. It does not interfere with vitamin absorption, but may increase slightly the secretion of mucus. Estimations of alkali reserve and of blood and urine chemistry remained normal throughout the course of treatment outlined in the present paper.

Since American authors claim 80 to 100% success for the use of synthetic resin, the present workers have given the drug to 15 patients with gastritis or peptic ulcer, 11 of whom had hyperchlorhydria. A total of 15 to 25 g. of resin in 3-hourly doses of 2 to 3 g. during the day and 5 g. at night (the high dosage is emphasized) produces a prompt and well-marked fall in total gastric secretion and in the levels of hydrochloric acid and pepsin as shown by histamine test meals. Secretion of acid is never completely abolished and in fact excess ions only are fixed, thus maintaining a physiological acid level in the stomach; symptoms consequently disappear rapidly. Test meals performed a few days after a 30-day course of treatment still produced a curve approaching normal in those with initial hyperchlorhydria. There was some improvement in the radiological appearance and function of the stomach, but little evidence of healing in those patients with an ulcer. *A. Paton*

2035. **Results of Peptic Ulcer Treatment with Protein Supplements**
L. M. MORRISON. *Review of Gastroenterology* [*Rev. Gastroent.*] **17**, 1058–1067, Nov., 1950. 2 figs., 17 refs.

A series of 20 ambulant patients with a history of proved peptic ulcer ranging from 4 months to 18 years were treated with a palatable proprietary preparation containing 60% protein, the remainder consisting of 27% carbohydrate, 1·3% fat, 6·3% minerals, and 5% moisture. The protein was mainly derived from milk, with a small proportion from egg (albumin) and soya bean. Following *x*-ray studies and gastric analysis the patients were fed for 7 to 21 days with 1½ oz. (46 g.) of this preparation in 6 oz. (170 ml.) of milk or water 1½-hourly. Night feedings were given as needed. On an average there was complete relief of pain in 48 hours as compared with 4½ days in a similar series treated conventionally and reported by the author in 1945. Titration curves are not given, but the buffering power of the protein supplement was apparently sufficient to prevent free acid appearing in the first hour after histamine. Changes in blood urea nitrogen and plasma protein levels and haematocrit and haemoglobin readings were not statistically significant. *Denys Jennings*

2036. **The Effect of Protein Hydrolysate Solutions on Gastric Acidity of Peptic Ulcer Patients**
D. C. H. SUN and T. E. MACHELLA. *Gastroenterology* [*Gastroenterology*] **16**, 577–585, Nov., 1950. 1 fig., 13 refs.

An aqueous solution of 30 g. of protein hydrolysate and 30 g. of " dextri-maltose " in 150 ml. of water was administered hourly by stomach tube to 20 patients with peptic ulcer and 2 with gastritis and a high gastric acidity. Total and free acidity was estimated and *p*H measured in specimens of gastric contents taken before each dose over a period of 14 hours, the stomach having been emptied before the first dose was given. No free acid was present in any of the specimens taken during the period of treatment in 11 cases, but in the other 11 free acid was present in 80 out of the 154 specimens.

To find out whether rapid emptying or dilution was the cause of this failure of the protein hydrolysate to buffer gastric acidity, 150 g. of barium sulphate was added to the mixture and the stomach examined radiologically in each case. There was a more rapid emptying rate in the unsuccessful group than in those cases in which achlorhydria was complete. Accordingly, the effect of giving atropine gr. 1/100 (0·65 mg.) every 3 hours subcutaneously was studied in 4 of the former group of subjects during a 9-hour period of hourly administration of the mixture; no free acid was present in 34 out of 36 specimens. The authors conclude that the success of such therapy depends on the concentration of the hydrolysate, its frequency of administration, and the rate at which the stomach empties. The use of atropine will reduce the proportion

in which free acid persists. The advantages and disadvantages of protein hydrolysate therapy, and some indications for its use, are stated with clarity. In stomal ulcer it is not advised, since severe "dumping" symptoms may occur. *K. Gurling*

2037. **Clinical and Roentgenographic Observations on Constipation in Patients with Peptic Ulcer**
A. LITTMAN and A. C. IVY. *Gastroenterology* [*Gastroenterology*] **16**, 674–679, Dec., 1950. 8 refs.

In many cases of peptic ulcer constipation is a complication which may call for undesirable modifications in treatment. The authors have tried to discover the main causes of the constipation in 31 patients by clinical observation and by radiography. Drugs used in therapy (especially calcium carbonate and aluminium gels) were responsible for the constipation in 61% of the patients; ulcer diets of low residue were probably the cause in only a few cases. Radiography of the upper abdominal tract did not reveal anything which would explain constipation, the amounts and distribution of the barium being subject to wide variations. *J. W. McNee*

2038. **A Study of the Alleged Deficiency of Gastric Mucin in the Stomach of Humans with Peptic Ulcer**
G. B. J. GLASS and L. J. BOYD. *Gastroenterology* [*Gastroenterology*] **16**, 697–715, Dec., 1950. 5 figs., 49 refs.

The theory that deficiency of gastric mucin is a causal factor in chronic peptic ulcer has been advanced repeatedly ever since Kaufman first propounded it in 1908. This theory—for which much evidence has been adduced—has been re-examined with great care and detail by the authors. Their conclusions are negative, neither defective secretion of mucin nor increased mucolysis being found in the 60 cases of peptic ulcer studied. Moreover, the hyperacidity in duodenal ulcer was due simply to hypersecretion and not to any disturbance of a buffering mechanism in the stomach provoked by deficiency of mucin. *J. W. McNee*

2039. **The Acid Reducing Mechanisms of the Normal Human Duodenum and an Observation on Duodenal Ulcer**
C. M. WILHELMJ, A. SACHS, B. SLUTZKY, and A. BARAK. *Gastroenterology* [*Gastroenterology*] **16**, 731–742, Dec., 1950. 5 figs., 24 refs.

A triple-lumen, double-balloon tube was used to isolate the secretions from the duodenum and to measure the rate at which acid instilled into the duodenum was neutralized. The tube was passed so that the distal balloon obstructed the intestine 10 inches (25·4 cm.) beyond the proximal balloon, which was anchored in the duodenal bulb. Some difficulty was always experienced in getting the second balloon past the pylorus, and in most of the subjects with duodenal ulceration this proved impossible. The attempt to discover whether, in such cases, there was an abnormality in the duodenal mechanism for acid neutralization was thus frustrated by technical difficulties. Useful facts were, however, obtained from studies on 4 normal controls; and the one patient with an active duodenal ulcer who was successfully intubated showed a lessened ability to neutralize hydrochloric acid, due to a diminished flow of duodenal juice, as compared with the controls. In the controls the quantity and alkalinity of the duodenal secretions, as well as the rate of acid neutralization, remained remarkably constant throughout 6 months of observation. Reduction in acidity following the introduction of 100 ml. 0·1 N. hydrochloric acid was achieved by dilution.

[The authors have clearly surmounted considerable technical difficulties in getting as far as they have. Those interested in the details should consult the original paper.] *J. Naish*

LARGE INTESTINE

2040. **Chloromycetin Therapy of Chronic Ulcerative Colitis—a One-year Study**
Z. T. BERCOVITZ. *Gastroenterology* [*Gastroenterology*] **16**, 19–24, Sept., 1950. 7 refs.

Progress has been studied over one year in 24 cases of chronic ulcerative colitis treated with chloramphenicol. The dosage of chloramphenicol used was 3 g. per day for one month initially. In cases of relapse shorter courses were used. No serious toxic effects were encountered, but dryness of the mouth, mild nausea, occasional giddiness, and a maculo-papular rash occurred. The effect of chloramphenicol on the stool culture of *Bacterium coli* and of streptococci was studied in 13 cases of ulcerative colitis, 8 normal individuals, and 5 patients in whom subtotal colectomy had been carried out. In all groups marked inhibition of both organisms occurred from the 1st to the 14th day of treatment, but thereafter there was a regeneration of the intestinal flora.

Clinical observation of the patients after chloramphenicol therapy was commenced revealed that 13 showed prompt and marked improvement. Four of these relapsed subsequently, but not to a degree as severe as at the outset of therapy. (Clinical estimation was based on the number of bowel movements, character of stools, sphincter control, abdominal discomfort, and sigmoidoscopy.) Three others were moderately improved, relapsing at intervals but not to an extent as severe as at the outset of treatment; 8 patients failed to respond.

The observed reduction in the faecal content of *B. coli* and streptococci following chloramphenicol treatment was not paralleled by the clinical response. In some cases there was marked inhibition with and without clinical improvement, and vice versa. In the 6 cases of ileostomy there was inhibition of growth of the organisms in the rectum with simultaneous improvement in the sigmoidoscopic appearances. This improvement was maintained up to 4 months after treatment.

Final clinical evaluation of the effects of chloramphenicol in this series can only be assessed after a period of 5 years, which will make allowance for the natural remissions and other variations in the clinical picture characteristic of this disease.

[The reappearance of *B. coli* and streptococcal flora

after the 14th day of chloramphenicol in spite of continued clinical improvement was presumably due to the development of resistant strains of these organisms. The author does not report whether *B. coli* and streptococci in relapsed cases which again responded to chloramphenicol were still resistant or not: but the available findings suggest that these organisms are not directly related to the active ulcerative process.] *M. Beaton*

2041. **Studies on Lysozyme in Ulcerative Colitis**
S. J. GRAY, R. W. REIFENSTEIN, E. P. CONNOLLY, H. M. SPIRO, and J. C. G. YOUNG. *Gastroenterology* [*Gastroenterology*] **16**, 687–696, Dec., 1950. 1 fig., 4 refs.

The essential cause of ulcerative colitis remains a puzzle, and all reasonable suggestions as to its aetiology seem worth investigating. Lysozyme has been regarded as a possible aetiological factor because there is a high lysozyme content in the stools in this disease. It might act by removing the protective surface mucus, thus laying the bowel wall open to damage by proteolytic enzymes or other agents. The acute phase of the disease was studied in 14 patients, in all of whom the lysozyme titre in the stools was high (average 109·4 units per g. as compared with the average in normal subjects of 4·8 units per g.). The chronic or inactive phase was studied in 19 patients (average lysozyme titre 11·9 units per g.). A detergent (" aerosol OT ") was used successfully to reduce the faecal lysozyme content in the 14 acute cases. The results were negative, and seem to show that lysozyme plays no significant part in the pathogenesis of ulcerative colitis. *J. W. McNee*

LIVER AND PANCREAS

2042 (*a*). **Clinical, Functional and Needle Biopsy Study of the Liver in Alcoholism**
M. SEIFE, B. J. KESSLER, and J. R. LISA. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 658–670, Nov., 1950. 6 figs., 24 refs.

Needle biopsy of the liver in 63 patients with chronic alcoholism revealed fatty metamorphosis in 47 cases, which was classified as " slight " in 10, " moderate " in 7, " marked " in 23, and " severe " in 7. No attempt was made to correlate these changes with the clinical or laboratory findings [which is perhaps unfortunate, as examination of the authors' figures shows that bromsulphthalein retention was abnormal in 10% of those with slight, in 28% of those with moderate, in 35% of those with marked, and in 86% of those with severe fatty metamorphosis. On the other hand, no such distinct correlation is to be found between the degree of fatty change noted and the results of the thymol turbidity test].

Histological evidence of cirrhosis was found in 21 patients, including 6 of the 7 with a palpable liver, 3 of the 4 with spider naevi, and the only patient with jaundice. These patients were nearly all steady, rather than intermittent, drinkers. Bromsulphalein retention and the plasma protein level were frequently abnormal in this group. In one-third of these cases cirrhosis was demonstrated histologically only at the second or third biopsy, as a result (according to the authors) of the focal distribution of fibrosis in early cirrhosis. No conclusions were reached regarding the incidence of cirrhosis in chronic alcoholism, since cases with advanced hepatic insufficiency were specifically omitted from the study. Repeated liver biopsy 1 and 2 weeks after withdrawal of alcohol and resumption of a normal diet showed a marked reduction of fat in all but 8 cases after one week and a further small decrease in the second week. The authors emphasize that no " specific " therapy was given, and claim that this rapidity of improvement has not been previously demonstrated. *Richard Terry*

2042 (*b*). **Use of Choline Supplements in Fatty Metamorphosis of the Liver. A Needle Biopsy Investigation in Human Beings**
B. J. KESSLER, M. SEIFE, and J. R. LISA. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 671–681, Nov., 1950. 6 figs., 25 refs.

Evidence is accumulating that treatment with a full diet is at least as effective as giving individual lipotropic substances in the treatment of fatty metamorphosis of the liver in alcoholism and other hepatic disorders. In this study 8 chronic alcoholic patients in whom fatty changes in the liver had failed to respond to diet alone were given choline chloride, 3·0 to 9·0 g. daily. Serial liver biopsies failed to show any increased fat clearance during the period of choline therapy. The authors concluded that choline is an unnecessary addition to the dietary therapy of fatty metamorphosis of the liver.

[These 8 patients were those mentioned in the preceding paper (see Abstract 2042 (*a*)) as failing to show improvement on normal diet. That each submitted to 5 serial liver biopsies is an indication of the slight degree of discomfort caused by this procedure.]

Richard Terry

2043. **The Diagnostic Value of the Serum Protein Picture in Liver Disease.** (Die diagnostische Verwertbarkeit des Serumeiweissbildes bei Erkrankungen der Leber)
F. HARTMANN and K. STEINEBACH. *Deutsches Archiv für Klinische Medizin* [*Dtsch. Arch. klin. Med.*] **197**, 568–577, 1950. 7 figs., 18 refs.

The authors discuss the results of the micro-electrophoretic examination of plasma protein patterns in 130 patients, comprising 62 cases of hepatitis, 37 of cirrhosis, 14 of cholangitis, 14 of metastasis, and 3 of acute liver dystrophy. A corresponding number of healthy subjects were also examined. The findings agree with those of most other workers. There is so often an increase in β and γ globulin and a fall in albumin levels in the blood in liver disease that hepatic damage should always be considered when such findings are obtained. The authors do not agree with those workers who find an increase in β-globulin level most frequently in liver disease; their results show quite clearly that the increase is mainly in γ globulin. The changes in the concentration of the latter, together with the fall in albumin concentration, constitute the most sensitive index of liver damage. The blood protein picture is not of much use

in differentiating the various types of liver lesion. It is, however, often valuable in estimating the severity and progress of the liver dysfunction. The synthesis of albumin and of fibrinogen is commonly affected early since these substances are produced almost exclusively in the liver; γ globulin is synthesized mostly (about 85%) in the liver, whereas α and β globulins are readily synthesized elsewhere in the reticulo-endothelial system. The production of these last is nevertheless dependent on carbohydrate and fat metabolism, the main site of which is again the liver.

Disturbances of protein metabolism in liver disease often present a regular progression, the faculty of synthesis falling off in the order: albumin, α, and β globulin; the progression is reversed in recovery. The high blood levels of γ globulin found in liver disease might suggest that its synthesis must be independent of liver function, but this is not so. Whatever the explanation, an increase in plasma γ-globulin level is associated with liver damage. *B. G. Maegraith*

2044. **Electrolyte Studies on Patients with Cirrhosis of the Liver**

W. J. Eisenmenger, S. H. Blondhelm, A. M. Bongiovanni, and H. G. Kunkel. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1491–1499, Nov., 1950. 6 figs., 9 refs.

Exhaustive balance studies were carried out at the Hospital of the Rockefeller Institute for Medical Research, New York City, on 41 patients suffering from cirrhosis of the liver. In 18 patients there was marked ascites and in 10 moderate ascites; in the remaining 13 there was no ascites. The patients with marked ascites had Laënnec's cirrhosis, and among the others were some cases of biliary or " postnecrotic " cirrhosis. Sodium and potassium content of the patient's food, serum, urine, sweat, and faeces were estimated by a flame photometer. The food and faeces were ashed before analysis, it being found that ashing at 500° C. was the best, although this left a certain amount of black material in the ashes. The residue after ashing at 800° C. was white, but [as might be expected] some of the sodium and potassium was lost. Care was taken to use the same pipettes for measuring the serum before the estimations and to check, by weighing the pipettes, the amount of serum delivered. Since some urines contained more than three hundred times as much potassium as sodium the question whether such large amounts of potassium interfered with the sodium estimations was studied, but the error was found to be small. Chloride concentration was also estimated in the food, serum, urine, and ascitic fluid, and nitrogen balance was estimated in some of the patients.

It was found that patients with severe ascites excreted extremely small amounts of sodium (their urinary excretion was usually below one mEq. daily and never above 4 mEq.), and excretion remained low even on a high intake of sodium. Those with ascites excreted by various means all the sodium they ate. Those with moderate ascites generally excreted less sodium in their urine than those who had no ascites [and it must be concluded that they retained some of the sodium they ate]. Serum sodium levels were low in patients with ascites (about 140 mEq. per 100 ml.), and low normal in the others. After paracentesis the serum sodium level fell even lower than before. If the intake of sodium was reduced to between 15 and 17 mEq. daily, the retention of fluid immediately stopped in those patients who were suffering from ascites. At the same time, however, potassium and nitrogen were retained in the body. Conversely, the serum sodium level increased and more sodium was excreted when patients with ascites began to improve, even before water balance could show that less water was being retained in the body. Since the saliva and sweat of patients suffering from ascites also contained less sodium than normal, the authors suggest that an overaction of the adrenal cortex may play a part in the retention of sodium in cirrhosis of the liver. This contention is supported by reference to some data which are to be published later. *E. M. Glaser*

2045. **The Use of Urecholine as a Stimulant of the External Secretion of the Pancreas**

G. C. Kyle, T. E. Machella, S. H. Lorber, J. T. Hilsman, J. G. Reinhold, and J. C. Brown. *Gastroenterology* [*Gastroenterology*] **16**, 285–293, Oct., 1950. 6 figs., 11 refs.

Urecholine (urethane of β-methylcholine chloride) has parasympathomimetic actions similar to those of " mecholyl ". The authors found that the subcutaneous injection of 10 mg. urecholine caused a twofold increase in the volume of the duodenal secretion as aspirated by a duodenal tube. This increase is explained as due to a simultaneous outpouring of pancreatic and biliary secretions, the latter increasing even in patients who had undergone cholecystectomy (18 with 18 controls). The volume of gastric secretion also rose after administration of urecholine. Reactions included sweating, salivation, abdominal cramp, and a desire to empty the bladder or rectum. *J. Naish*

2046. **Study of Pancreatic Serum Enzymes following Secretin Injection in Pancreatic Affections**

M. S. Lopusniak and H. L. Bockus. *Gastroenterology* [*Gastroenterology*] **16**, 294–308, Oct., 1950. 6 refs.

Among the many tests of pancreatic function now being tried those that appeal most to the clinician are the simplest. The estimation of the serum levels of pancreatic enzymes is of value in the diagnosis of acute pancreatitis. The authors found that patients recovering from acute pancreatitis had high serum levels of amylase and lipase following the intravenous injection of 80 units of secretin. On the other hand, eight patients with gross pancreatic insufficiency due to destructive changes in the gland showed no serum enzyme response to secretin. In patients with carcinoma of the pancreas and those with idiopathic steatorrhea the responses were variable.

[It is evident that such a secretin test, though simple, is not, by itself, informative enough.] *J. Naish*

See also Section Pathology, Abstract 1874.

Endocrine Disorders

2047. **Hyperfolliculinism and Hyperthyroidism.** (Hyperfolliculinie et hyperthyréose; étude physio-pathologique, clinique et thérapeutique)
J. OLMER, G. ERLANDE, and E. ABIGNOLI. *Presse Médicale* [*Pr. méd.*] **58**, 1342–1346, Nov. 29, 1950.

In this paper from the Marseilles Faculty of Medicine the authors discuss the interrelationship of the pituitary–ovarian and pituitary–thyroid axes. Attention is drawn to the transitory enlargement of the thyroid which may occur during puberty, the premenstrual phase, and pregnancy, and which may precede the menopause. This enlargement is believed to be compensatory, in response to an increased need for thyroxine. It is suggested that the enlargement may persist and lead to the syndrome of thyrotoxicosis. The authors seek to differentiate a group of women in whom the syndrome of hyperfolliculinism is followed by a mild thyrotoxicosis which may eventually become more severe. Good results are claimed from treatment aimed at suppressing pituitary activity. They gave 3 to 5 injections of testosterone propionate (25 mg.) between the 17th and 26th days of the menstrual cycle, for 3 cycles. One free cycle was allowed and treatment then started again with methyl testosterone orally.

[The number of cases on which these observations are based is not stated.] *G. Ansell*

See also Section Pathology, Abstracts 1880–81.

2048. **Further Studies on Pseudo-hypoparathyroidism. Report on Four New Cases**
H. ELRICK, F. ALBRIGHT, F. C. BARTTER, A. P. FORBES, and J. D. REEVES. *Acta Endocrinologica* (*Copenhagen*) [*Acta endocrinol., Kbh.*] **5**, 199–225, 1950. 13 figs., 11 refs.

Pseudo-hypoparathyroidism is a syndrome in which the changes characteristic of idiopathic hypoparathyroidism—low blood calcium level and high blood phosphorus level—are present, but biopsy of the parathyroid glands reveals hyperplastic changes. It appears that there is no lack of parathyroid hormone, but rather a resistance of the body tissues to its action. In the present paper from the Massachusetts General Hospital 4 new cases are described and 10 other cases from the literature are reviewed. The patients were typically short and thick-set with a rounded face. There was usually evidence of dyschondroplasia manifesting itself particularly as shortening of one or more metacarpals or metatarsals. In addition to the calcification of the basal ganglia characteristic of idiopathic hypoparathyroidism, the patients commonly showed subcutaneous areas of calcification or metaplastic bone formation. In several patients there was mental retardation. The presenting symptoms were convulsions or tetany due to the hypocalcaemia; these responded to treatment with dihydrotachysterol.

The authors consider that this is a genetic disorder involving three genes, one causing end-organ resistance to parathyroid hormone, one dyschondroplasia, and one subcutaneous calcification. Any of these three disorders may occur independently. It is also suggested that idiopathic hypoparathyroidism is closely related to myositis ossificans progressiva, since both conditions show a tendency to dyschondroplasia and ectopic ossification. *G. Ansell*

2049. **Pharmacological and Clinical Results with ACTH in 112 Cases**
F. PAULSEN. *Acta Endocrinologica* (*Copenhagen*) [*Acta endocrinol., Kbh.*] **5**, 292–326, 1950. 1 fig., bibliography.

The author has correlated the results obtained with adrenocorticotrophic hormone (ACTH) in the treatment of 112 patients in various Scandinavian clinics. The doses given were smaller than those "used by most American workers in similar investigations". It is claimed that daily doses of 20 to 25 mg. were effective in adults provided this was divided into 4 or 5 injections. The threshold value for a single dose appeared to be in the region of 10 mg., and was sufficient to produce a 50% reduction in the eosinophil count. The physiological dose required to stimulate a patient with post-operative adrenal collapse was even lower (1 to 5 mg.). Children under 3 years and several children under 7 years were refractory to relatively high doses of ACTH, probably due to incomplete development of the adrenal cortex. In these children pretreatment with chorionic gonadotrophin or repeated small doses of ACTH enabled a response to be obtained with subsequent therapeutic doses of ACTH. Results obtained in the various diseases treated are briefly discussed. ACTH changes the viscosity of the bronchial mucus in status asthmaticus, and the authors believe that the mechanism of action of the drug is linked with an effect on the polymerization of carbohydrates and especially of mucopolysaccharides.

[It is not possible to abstract this paper adequately, and it should therefore be read in the original by those interested.] *G. Ansell*

2050. **Studies of Adrenal Cortical and Anterior Pituitary Function in Elderly Men**
D. H. SOLOMON and N. W. SHOCK. *Journal of Gerontology* [*J. Gerontol.*] **5**, 302–313, Oct., 1950. 6 figs., 38 refs.

Adrenal cortical and anterior pituitary function was studied in two groups of men: 30 aged 20 to 44, and 26 aged 61 to 89. The biochemical and haematological response to 18 mg. of adrenocorticotrophic hormone (ACTH) was taken as a measure of the secretory capacity of the adrenal cortex; while the response to 0·4 mg. of adrenaline was used as a test of the capacity of the anterior pituitary to secrete ACTH. As the fall in the

eosinophil count induced by 18 mg. of ACTH was the same in both groups, it is concluded that the ability of the adrenal cortex to secrete cortisone or " S " steroids is unimpaired in old age. The increase in uric acid excretion rate in response to ACTH was significantly smaller in the aged; this is attributed to a renal defect. The increase in the potassium excretion rate was also significantly smaller in the older men. The only significant difference in the two groups following adrenaline administration was the greater eosinophil depression in the young.

[This is a well-documented paper which should be read in the original. The authors' deductions can, however, be criticized on logical grounds. For example, the stated object of the adrenaline test was to measure the secretory capacity of the anterior pituitary: yet when the response to this test was smaller in the aged than in the young they reject the logical inference. Their argument that " the long-term pituitary output of ACTH in the aged cannot be notably reduced since the adrenal cortex retains its responsiveness to ACTH ", is a *non sequitur*. Their case for a renal mechanism causing impaired uric acid diuresis in the aged in response to ACTH is not proved.] *P. D. Bedford*

2051. **Experimental and Clinical Comparison between Responses to Adrenaline and to ACTH in Thorn's Test**
(Comparaison expérimentale et clinique entre l'épreuve de Thorn à l'adrénaline et à l'A.C.T.H.)
B. M. DE FOSSEY and G. H. DELTOUR. *Annales d'Endocrinologie* [*Ann. Endocrinol., Paris*] **11**, 341–360, 1950. 4 figs., 19 refs.

The response to the standard Thorn test, in which the response of the eosinophil count to injection of adrenocorticotrophin (ACTH) is taken as a measure of adrenal cortical function, was compared with that to the modified test employing adrenaline in place of ACTH. In normal subjects there was marked eosinopenia and an increased excretion of uric acid on injection of 25 mg. of ACTH, as also in a group of 3 cases of " pseudo-Addisonian asthenia ", whereas injection of 1·5 mg. of adrenaline produced a fall in eosinophil count but no change in uric acid output. In 4 cases of true Addison's disease, however, ACTH injection was not followed by a fall in eosinophil count or an increase in the uric acid/creatinine ratio, that is, Thorn's test was negative and in accordance with the clinical diagnosis, whereas administration of adrenaline to these patients provoked considerable eosinopenia, despite the reduction in adrenocortical function.

The authors then investigated these responses in the albino rat. They found that the eosinophil count of the normal animal was subject to wide spontaneous variations, attributable to the stress of handling and other alarm stimuli and rendering difficult the interpretation of the experimental results. Adrenalectomized rats were less sensitive to stress. In the intact rat the fall in eosinophil count was marked and consistent during the hour following ACTH injection, whereas adrenalectomized rats showed minimal or no response. The effect of adrenaline in both groups was so variable as to defy interpretation. The number of circulating eosinophils is evidently influenced by sympathetic excitation as well as by activity of the adrenal cortex.

The authors conclude that the Thorn test with ACTH has great value in estimating suprarenal function, but that the modified test with adrenaline is unreliable.

Nancy Gough

2052. **Development of Hypercholesteremia during Cortisone and ACTH Therapy**
D. ADLERSBERG, L. SCHAEFFER, and S. R. DRACHMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 909–914, Nov. 11, 1950. 3 figs., 5 refs.

An investigation is reported of the serum cholesterol level in a number of patients undergoing treatment with cortisone or adrenocorticotrophin (ACTH) for a wide variety of diseases. Total and esterified cholesterol was determined by the method of Sperry and Schoenheimer.

Of 26 courses of cortisone acetate administered to 22 subjects, 21 gave rise to high serum cholesterol levels, both total and esterified. Elevation of both these levels also occurred in 15 out of 21 courses of ACTH therapy. Of 8 patients who received hormone treatment for longer than 60 days 7 developed hypercholesterolaemia (over 280 mg. per 100 ml.); the incidence was much lower in those patients on shorter courses. If hormone therapy was reduced or terminated the serum cholesterol level often fell with the recurrence of symptoms, and on resuming treatment the amelioration of symptoms was usually accompanied by elevation of the cholesterol level. Consistent parallelism between the serum phospholipid and cholesterol levels was observed. Cortisone appeared to be more effective than ACTH in producing sustained hypercholesterolaemia. Investigation of the families of some of the patients concerned showed that hereditary hypercholesterolaemia was present in only 2 of the 8 subjects undergoing prolonged hormone treatment.

It has now been demonstrated that prolonged administration of adrenal cortical agents (cortisone and ACTH) can produce sustained hypercholesterolaemia, as can suppression of normal thyroid function. Abnormal distribution of body fat and elevation of serum cholesterol level, characteristics of Cushing's syndrome, are frequently observed in patients undergoing long courses of treatment. Moreover, premature atherosclerosis (associated with hypercholesterolaemia), often observed in Cushing's syndrome, may be induced by such treatment. Animal experiments to test this possibility are in progress.

Nancy Gough

2053. **Effect of Cortisone on Early Fibrosis of the Liver in Rats**
K. ATERMAN. *Lancet* [*Lancet*] **2**, 517–519, Nov. 11, 1950. 4 refs.

Twenty female Sprague–Dawley rats weighing 125 g. were fed *ad lib.* with " Purina chow ". All were injected with carbon tetrachloride (0·1 ml. subcutaneously, twice weekly), according to the schedule of Cameron and Karunaratne (*J. Path. Bact.*, 1936, **42**, 1). The total

number of injections varied from 23 to 33 in the different groups of animals. Seven animals received large doses of cortisone subcutaneously which were given during the period of injection of carbon tetrachloride (15 mg. a day for 4 days, followed by 10 mg. a day for 8 days in one group of 4 rats; 15 mg. a day for 4 days followed by 7 mg. a day for 9 days 3 weeks later in another group of 3 rats). Animals were killed at times varying from 3 to 4 days after the last dose of carbon tetrachloride up to 13 days afterwards in one of the control groups; rats treated with cortisone were killed 2 days after the last injection. All were starved for a day before killing. Tissues were examined after fixing by freezing and in formalin–Zenker; Hotchkiss, Mallory–azan and Bielchowsky stains were used.

Results indicated that there was some inhibition of the formation of fibrous tissue in the livers of rats receiving cortisone, sections of which in 5 out of 7 animals showed considerably less collagen and reticulin than in the rats given carbon tetrachloride alone; there was also some reduction of round-cell infiltration. Granulomatous nodules were present in one animal, which also displayed fibrosis. The amount of glycogen in the liver cells was considerably increased in the treated animals. The effects of carbon tetrachloride were similar to those described by Cameron. The general effects of cortisone were those noted by others—loss of weight and decrease in size of spleen and suprarenals.

In a short discussion the author considers the possible mechanisms involved in the apparent inhibition of fibrosis in the animals receiving cortisone.

[Presumably this very interesting paper is in the nature of a preliminary note. As it stands, without photomicrographs of the experimental results, the discussion seems to the abstracter to outweigh the presented evidence.] *B. G. Maegraith*

2054. **The Effect of Cortisone on the Excretion of 17-Ketosteroids and Other Steroids in Patients with Congenital Adrenal Hyperplasia.** (Die Wirkung von Cortison auf die Ausscheidung der 17-Ketosteroide und anderer Steroide bei Patienten mit kongenitaler Nebennierenhyperplasie)

L. Wilkins, R. A. Lewis, R. Klein, and E. Rosemberg. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **5**, 418–425, Nov., 1950. 4 refs.

Observations were made on 6 children, aged 2 to 15 years, with congenital adrenal hyperplasia, 4 of them female pseudohermaphrodites, 2 of them boys with macrogenitosomia praecox. Cortisone markedly reduced the urinary 17-ketosteroid excretion. In all except one 25 mg. daily was as effective as 50 or 100 mg., reducing the 17-ketosteroid output from 10 to 48 mg. to between 4 and 8 mg. in 24 hours, but the response was more rapid when the larger doses were used (within 4 to 6 days as opposed to 6 to 15 days). The urinary 17-ketosteroid output was reduced so long as treatment was continued (up to 48 days in one case), but rose again 10 days after it was discontinued, returning to the initial level within a further 7 days. Urinary oestroid excretion was high initially, fell during treatment, and rose again subsequently. Urinary 11-oxysteroid levels were raised initially and tended to fall during treatment, but the results were less constant, probably because a portion of cortisone is excreted in this fraction. In one case the depression of 17-ketosteroid level was interrupted by an abrupt transient rise for a few days, associated with a febrile cold. Treatment was not sufficiently prolonged to produce any effect upon the virilism, except for the relief of a persistent and painful erection of the clitoris in one case following its partial amputation.

No side-effects were observed. There was a moderate increase in nitrogen excretion and diminution of weight gain on a constant diet. Serum electrolyte levels and sugar tolerance were not affected. In a 23-month-old boy with macrogenitosomia praecox and symptoms of Addison's disease (already controlled with high salt intake and deoxycortone) urinary sodium and blood electrolyte levels were normal during administration of cortisone, but there was a marked sodium diuresis immediately the cortisone was discontinued. The other boy with macrogenitosomia praecox had a blood pressure of 150/100 mm. Hg before treatment, which rose to 210/140 mm. on the 10th day of cortisone administration but returned to the initial level when treatment was discontinued. *Robert de Mowbray*

2055. **Hypothalamic Lesion with Diabetes Insipidus. Treatment with 8-Carboxy-3-hydroxy-2-phenylcinchoninic Acid.** (Hypothalamus-laesion med diabetes insipidus, behandlad med 8-carboxy-3-hydroxy-2-phenylcinchoninsyra)

P. Wising. *Nordisk Medicine* [*Nord. Med.*] **44**, 1838–1840, Nov. 17, 1950. 1 fig., 5 refs.

The case is reported of a female patient aged 38 who had had acute encephalitis 3 years before the present study was made at the Karolinska Institute, Stockholm, and who was now suffering from symptoms suggesting a widespread lesion of the hypothalamus involving (chiefly) its anterior and lateral parts. She suffered from hyperthermia and hypersomnia, outbursts of fear and rage, paroxysms of hunger, diarrhoea and vomiting, and increased capillary fragility with oedema. Her urine output was 6 to 14 litres per day, her systolic blood pressure varied from less than 100 mm. to 200 mm. Hg, and her blood sugar level was 62 mg. per 100 ml. on one occasion. There was no evidence of endocrine disturbance. Pituitary extract, "pitressin" tannate, and amidopyrine were all tried, but while all reduced her urine volume, they made her other symptoms worse.

She was then given a treatment developed by Marshall and his associates (*Bull. Johns Hopk. Hosp.*, 1950, **86**, 89) consisting of the administration of 8-carboxy-3-hydroxy-2-phenylcinchoninic acid in doses of 40 μg. per kg. body weight 3 times daily by mouth. On the first day of this treatment the 24-hour urine volume fell from nearly 9 to 5 l., and on the third day of treatment it fell to 3 l. The drug was given in similar doses over a period of 4 months, the patient's urine output remaining between 2 and 3 l. daily during the first 3 months and between 3 and 4 l. daily during the fourth month. The side-effects of this treatment were negligible. *E. M. Glaser*

Dermatology

2056. **Contact Dermatitis due to Synthetic Resins in Shoe Linings**
J. W. JORDON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 671–680, Nov., 1950. 2 figs., 21 refs.

The author reports 47 proved cases and 29 suspected cases of dermatitis due to the use of synthetic resins as partial linings in shoes. The characteristics of the dermatitis, the results of patch tests, and the response obtained after the offending shoes were discarded are described. Investigation of many resins suggested that potency of a basic resin in producing dermatitis depends on the degree of polymerization. The use of a standard series of resins for patch tests proved of little value; sensitivity had to be tested to the compound with which the patient actually came into contact.

During the discussion the part played by hyperhidrosis, chemicals such as phenol and chrome, and fungi in infections of the feet was emphasized; too much stress should not be laid on more recently discovered sensitizers. *G. B. Mitchell-Heggs*

2057. **Infantile and Atopic Eczema from Injury to the Skin by Overcare and Overtreatment**
L. E. GAUL and G. B. UNDERWOOD. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 739–752, Nov., 1950. 2 figs., 7 refs.

The authors discuss the results of over-treatment of the skin with soap and water and various skin applications. They stress the importance of preserving the vernix caseosa in newborn babies and the damage inflicted on the skin of older children by the use of too much soap and the application of preparations containing sensitizing agents. The effects of dermatitis from sensitization on the adaptation of the skin to changes of temperature and humidity are discussed and preventive measures suggested. *S. T. Anning*

2058. **Dyschromic Spirochaetosis.** (La spirochetosi discromica)
S. PAMPIGLIONE. *Rivista di Parassitologia* [*Riv. Parassit.*] **11**, 233–259, Dec., 1950. 4 figs., bibliography.

Biocca, of Brazil, introduced this name in 1945 for the disease which has been known as pinta and under a wide variety of other, mostly local, designations. The condition is common among the inhabitants of hot, humid villages and small towns, generally situated along the river banks, in the equatorial territories of the American continent. In cases recorded from elsewhere the diagnosis is considered doubtful. The incidence is very heavy in some communities—60 to 70% on the island of Guadaloupe. American Indians, negroes, and half-castes are the races usually affected, possibly due to their low social and hygienic standards. Both sexes appear equally affected, mostly between the ages of 30 and 40 years; susceptibility to the infection is most marked between the ages of 15 and 40.

The incubation period, averaging 10 to 15 days, may vary from 7 to 30 days. Onset is insidious and the primary sore, at the point of inoculation, generally a habitually exposed part of the body surface, is accompanied by itching, which continues into the secondary stage. This develops in 2 to 5 months after infection, with rash, pyrexial attacks, and lymph-node enlargement. By the end of 1 to 5 years the tertiary stage has set in with a characteristic range of discoloured patches on the skin. Spontaneous local healing may lead to scarring and white patches. Lymph-node enlargement is also common in this tertiary stage and the heart and blood vessels may be affected.

Treponema caratum (Brumpt, 1939) is the infective agent. The causal relationship has been confirmed by various Latin American workers by inoculating themselves and a number of volunteers. Blood-sucking insects may play a part in transmission by biting or by the host's oral route (engorged insects being eaten with the food). A more direct skin inoculation appears to be the more common mode of spread and in this, ritual dancing (mutual flogging) as well as criminal practices have been found to play an important part in regions of the Rio Negro and Rio Içana, Brazil, which Biocca visited in 1944. Venereal spread has not been demonstrated. Arsenic, bismuth, mercury, the iodides, and penicillin provide specific remedies and, in the absence of tertiary changes in the heart and blood-vessels, the prognosis is favourable. *J. Cauchi*

2059. **Tropical Ulcers**
H. A. POINDEXTER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 624–631, Nov., 1950. 1 ref.

A study of the microbic flora of 400 cases of tropical ulcers in Liberia is presented. During the rainy season organisms of the greatest prevalence in the ulcers were *Staphylococcus aureus* or *Staph. albus* and *Borellia vincentii* with the fusiform bacilli. During the dry season the organisms of greatest prevalence in the ulcers were *Corynebacterium* species and *Staphylococcus aureus* or *Staph. albus*. Many of the corynebacteria were proved to be *Corynebacterium diphtheriae* by culture and inoculations.

When the microbic flora of tropical ulcers of more than 5 cm. in diameter were determined and more specific therapy given, the average healing time was reduced by 2 to 2½ months even when compared with the results with such widely used routine treatments as bismuth subsalicylate and oxophenarsine injections or the oral and local use of sulfonamides when applied indiscriminately, as is frequently done in Liberia in tropical ulcer cases.—[Author's summary.]

2060. **Alopecia Areata: a Clinical Study**
I. ANDERSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1250–1252, Dec. 2, 1950. 10 refs.

Alopecia areata is presumed to have an incidence of 2 to 3%. The present paper is based on 114 cases seen during 2 years, including 24 cases of the total or universal varieties. There was no difference in sex incidence, nor in regard to hair colour. The disease occurred at all ages but was commonest in children. The site of the primary patch was markedly different in the sexes, for 35 of the males had occipital patches and 15 fronto-vertical, whereas the females showed a reversed distribution, namely, 15 occipital and 31 fronto-vertical. The higher incidence of primary occipital involvement in boys compared with girls is strikingly similar to that reported in ringworm of the scalp. The fact that in 19% of cases alopecia areata had occurred in another member of the family is not regarded as conclusive evidence of a familial tendency. There was only one case with a multiple family history (grandparent and father).

The commonest precipitating cause was mental shock or acute anxiety. Focal sepsis appeared of no special importance. An associated vitiligo was found in 4% of cases. Interesting nail changes were quite common, especially in severe cases, and consisted either of longitudinal striations with a serrated nail edge or of pitting resembling that seen in psoriasis. These may indicate a very bad prognosis.

Prognosis in the early stages is difficult, but probably less than 1% suffer permanent ill-effects. The outlook is much worse when the disease has its onset before the age of 10. Cases of alopecia totalis without loss of body hair may recover even after a year or longer, but alopecia universalis is nearly always permanent. The author feels that patients with small recurrent patches usually recover eventually, while some of the ophiasis type progress to permanent complete baldness.

The aetiology of alopecia areata remains unknown; it could be either a disorder of general adaptation with the hair as a " target area ", or it might possibly be a virus disease. *E. W. Prosser Thomas*

2061. **Role of Parenteral Multivitamin Therapy in the Treatment of Acne**
P. R. KLINE. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 661–665, Nov., 1950. 17 refs.

The interrelationship of vitamins and the endocrine glands, the effect of vitamins on the pilo-sebaceous apparatus, and the past failure of hormonal treatment in acne vulgaris are discussed. A method of administering vitamin A and its absorption, storage, utilization, and excretion are described. The clinical response to an aqueous multivitamin solution administered intramuscularly over a period of 8 months to 25 patients with acne vulgaris was excellent. Many cases unresponsive to usual therapeutic procedures showed prompt and consistent progress. The solution was well tolerated in over 500 injections and there was no pronounced tendency to relapse after its parenteral administration was discontinued. *G. B. Mitchell-Heggs*

2062. **Heredity and Leg Ulcers**
S. T. ANNING. *British Medical Journal* [*Brit. med. J.*] **2**, 1305–1307, Dec. 9, 1950. 3 figs., 30 refs.

In this paper the author first reviews the literature on the subject and then presents his findings in a series of 525 cases seen at Leeds General Infirmary. These cases were first divided into thrombotic and non-thrombotic groups. The series was then further subdivided into different aetiological groups. In the thrombotic series of cases there was a positive family history in 25%. It is pointed out that hereditary factors may have played some part in causing the thrombosis, so that this figure does not represent that to be found in the general population. In the thrombotic group 53·4% of the patients with ulcers caused by post-partum thrombosis gave a positive family history. It is noted that the mothers of 10 of the patients and the sisters of 2 of these 10 had also suffered from post-partum thrombosis. It is pointed out that special precautions seem to be indicated in parturient women with a family history of varicose veins, leg ulcer, or thrombosis, especially if the confinement is difficult. Among the other patients in the thrombotic group, those with ante-partum thrombosis and thrombosis due to treatment of varicose veins, operation on the leg, and to unknown causes had a higher incidence of positive family history than was expected. In " silent " thrombosis and thrombosis from recumbency heredity seems to play a doubtful part.

In the non-thrombotic groups heredity is clearly of importance in ulcers due to varicose veins alone. A positive family history was present in 89·9%.

The number of patients with primary arteriosclerotic ulcers was small, but of these a large proportion gave a family history of leg ulcers without varicose veins. It is notable that, apart from the arteriosclerotic group, the proportion of patients with a family history of ulcers only was small compared with that of patients with a family history of varicose veins. Primary varicose veins seem to be the common factor in the family history, when positive, of most patients with leg ulcers of the post-thrombotic and the varicose types. *H. S. Laird*

2063. **A New Case of Familial Pachydermia Plicata (Cutis Gyrata) with Pachyperiostosis of the Extremities.** (Un nouveau cas familial de pachydermie plicaturée (cutis gyráta) avec pachypériostose des extrémites)
A. FRANCESCHETTI, R. GILBERT, D. KLEIN, and P. WETTSTEIN. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1301–1306, Dec. 9, 1950. 8 figs., bibliography.

A good description is given of this familial malady, which occurs mainly in men. Periosteal bone is laid down symmetrically in the long bones and there is thickening of the skin, especially of the face, scalp, hands, and feet. The skin tends to be greasy and may be so wrinkled as to give the face a bulldog appearance. The fingers and toes are fleshy and have a type of clubbing which causes the nails to resemble watch glasses. No characteristic biochemical changes have yet been found. The relationship to acromegaly and hypertrophic pulmonary osteoarthropathy is discussed. The variations

of this syndrome which may be found in different cases are described, with a good review of the literature and photographs of 2 cases. *G. S. Cockett*

2064. **Failure of ACTH (Adrenocorticotropic Hormone) in the Treatment of a Case of Mycosis Fungoides. Report of a Case**
L. TULIPAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 349–350, Nov., 1950. 1 ref.

2065. **The Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on the Course of Disseminated Lupus Erythematosus and Periarteritis Nodosa**
R. A. CAREY, A. M. HARVEY, and J. E. HOWARD. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 425–460, Nov., 1950. 11 figs., 14 refs.

The authors describe their experience with adrenocorticotrophic hormone (ACTH) in 8 patients suffering from disseminated lupus erythematosus. The initial daily dose was 100 mg., reduced gradually to 20 or 10 mg., and the period of treatment was 15 to 68 days. To 4 other patients suffering from the same condition the authors gave cortisone in initial doses of 200 to 400 mg., reduced gradually and continued for 11 to 18 days. The patients had had the disease for periods varying from 1 month to 8 years, with an average of 2 years. In all cases there were systemic features as well as skin lesions. All the patients responded immediately and dramatically to administration of ACTH or cortisone, the temperature becoming normal and the joint pains disappearing within 24 hours. An increased sense of well-being, loss of fatigue, and increase in appetite were noted, together with recession of skin lesions, absorption of pleural and pericardial effusions, and subsidence of palpable lymph nodes. Temporary relapse occurred in 5 cases, with recrudescence of fever and of skin and joint lesions, when the dose of ACTH was reduced to less than 40 mg. daily. This " rebound phenomenon " subsided spontaneously in 7 to 15 days. Up to the time of the present report 5 patients had had remissions lasting from 3 to 11 months. In 5 there was a relapse of varying severity from 7 days to 4 months after treatment; 2 of these patients had a further course of treatment, which was followed by a relapse after 7 days in 1 case and a remission lasting 6 months in the other. There were 2 deaths, one from empyema, the other from renal insufficiency.

In 5 other patients (4 of whom received ACTH and 1 cortisone) with predominant skin manifestations and no significant systemic involvement the response was less satisfactory. There was some 40 to 50% improvement in chronic lesions, but relapse occurred soon after treatment was discontinued.

Neutrophilia and lymphopenia followed administration of ACTH or cortisone, but eosinophils were already greatly reduced in number or absent before treatment was begun in most cases and therefore did not form a satisfactory index of response. The erythrocyte sedimentation rate fell to normal in 7 cases and was unchanged in 10, there being a quantitive relation with the degree of clinical response and the duration of remission. Hargreaves's " L.E." cells were reduced in number in the peripheral blood during treatment, and serum gammaglobulin concentration fell strikingly.

One case of periarteritis nodosa is also reported in which recurrent episodes of the disease each responded in turn to three separate courses of ACTH, as shown both clinically and by serial muscle biopsy.
Robert de Mowbray

2066. **Psychiatry and the Skin**
R. M. B. MACKENNA, E. WITTKOWER, and H. J. SHORVON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 797–804, Nov., 1950. 14 refs.

MacKenna, in opening the discussion, pointed out that skin diseases may cause great anxiety; thus some men with alopecia areata associate it fearfully with impotence. On the other hand, psychogenic factors are important in the aetiology of many dermatoses, such as alopecia areata, dyshydrosis, and lichenification (" neurodermatitis "). Neurodermatitis of the nape of the neck in middle-aged women, however, although morphologically identical with circumscribed neurodermatitis of other sites, is peculiar in being confined to menopausal and post-menopausal women. It is better called " lichen simplex chronicus " and is probably largely endocrine in origin, usually in a seborrhoeic subject.

Wittkower reported on the psychiatric examination of more than 400 patients with various dermatoses. Patients with pruritus vulvae can be classified into the " shouldn'ts ", the " won'ts ", and the " can'ts ". The " shouldn'ts " feel guilty about their sex life; the " won'ts " feel bound to cohabit with a man they loathe; and the " can'ts " are denied sexual gratification or fertility. At a deeper level, in many, there is a revival of guilt concerning infantile incest phantasies. Female patients with pruritus ani are frigid; males often have disordered sexual function. Endogenous eczema occurs in emotionally insecure people who feel the need of affection and protection; in a few cases the site of eczema may be symbolically determined. Patients with rosacea are usually shy and have a deep-seated sense of guilt, rosacea being equivalent to a permanent blush. Of 74 patients with ano-genital pruritus, eczema, and rosacea who were treated by brief psychotherapy, 60 derived benefit from it. Those with rosacea responded most, and those with pruritus ani least, to this treatment.

Shorvon described his use of abreaction to relieve tension in patients with dermatoses. Abreaction in obsessional patients is helped by the intravenous injection of 30 mg. of methylamphetamine (" methedrine "), " sodium amytal ", 6 grains (0·4 g.) by mouth, being given some hours later. Hysterical and anxious patients do well with ether abreaction. Inhalation of a mixture of 30% carbon dioxide and 70% oxygen until there is generalized muscular twitching is sometimes of use; at least 20 treatments, given 2 or 3 times weekly, are needed. In general, the results of treatment are encouraging. *E. Lipman Cohen*

See also Section Psychiatry, Abstract 2110.

Venereal Diseases

2067. **The Use of Oral Penicillin in a Buffered Sulfonamide Mixture in the Treatment of Acute Gonorrheal Urethritis**

P. B. JOHNSON, J. H. SEABURY, and D. M. DUMVILLE. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 83–87, Jan., 1951. 1 fig., 8 refs.

The effect of combining oral penicillin with oral sulphonamides was investigated on the cure rate of acute gonorrhea. Over a 5-day period a total of 500,000 units of penicillin was given by mouth together with 16 g. of a sulphonamide mixture. The mixture was composed of 2 g. of sodium citrate, 0·5 g. of sulphadiazine, and 0·5 g. of sulphamerazine in 10 ml. of water. Of 47 patients receiving the mixture 44 were cured. When 300,000 units of penicillin was given together with the sulphonamides the cure rate was lowered. A similar result was obtained when 500,000 units was given alone. There is no evidence that the addition of the sulphonamides to the penicillin increases either the blood level of the antibiotic or the duration of the penicillin in the blood. It is concluded that the sulphonamides act synergistically with the penicillin.

[No mention is made of the sensitivity of the gonococci to sulphonamides.] *G. M, Findlay*

2068. **Oral Terramycin in the Treatment of Gonorrhea in the Male**

R. C. V. ROBINSON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 587–589, Nov., 1950. 5 refs.

Terramycin, an antibiotic prepared from *Streptomyces rimosus*, was given by mouth to 24 patients with gonorrhoea, all but one of whom were negroes. After observation for one week there were 3 failures among 6 patients given a single dose of 1 g., but among the remaining 18, who were given 2 g., there were only 4 failures. Three patients vomited ½ to 4 hours after swallowing the drug, and 2 of them were unable to retain a second dose and were treated again with penicillin.

R. R. Willcox

2069. **Nongonococcal Neisserian Strains Isolated from the Genitourinary Tract**

J. JOHNSTON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 79–82, Jan., 1951. 6 refs.

The presence of non-pathogenic *Neisseria* in the urinary tract of healthy adults is described. Of 43 cultures 12 were identified as *Neisseria subflava* and 31 as *N. sicca*. Most of the plates containing the organisms showed only a very small number of colonies per plate and with one exception every attempt to isolate them in subsequent cultures from the same patient failed. The non-pathogenic *Neisseria* showed larger, more pigmented, colonies and gave the oxidase reaction as a black ring at the periphery of the colonies. In stained smears the cocci showed great diversity of size and were often arranged in close packets. The colonies were easy to isolate as they were not overgrown by contaminants.

G. M. Findlay

2070. **The Cultivation of Pleuropneumonia-like Organisms from the Human Genitourinary Tract with Reference to their Possible Venereal Transmission**

H. E. MORTON, P. F. SMITH, and P. R. LEBERMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 14–17, Jan., 1951. 10 refs.

A standard medium for the isolation of pleuropneumonia-like organisms is described. It consists of "50 g. of 'bacto-beef' heart for infusion in 1,000 ml. distilled water, to which is added 1% 'bacto-peptone', 0·5% sodium chloride, and 1·5% agar". The *p*H is adjusted to 7·8% before sterilization in the autoclave. Before the medium is poured into plates, 25% sterile human ascitic fluid or 10% mammalian serum is added to the cooled (50° C.) melted basal medium: crystal violet 1 in 100,000 and potassium tellurite 1 in 50,000 are inhibitory to most bacterial contaminants. A total of 85 patients, 14 females and 71 males, were examined, and 7 women and 14 men yielded positive cultures. There was arthritis associated with conjunctivitis, urethritis, or prostatitis in 10 patients; prostatitis associated with iritis in 2; and urethritis associated with iritis in 2. Of these 14 patients 7 gave positive cultures. The possible venereal transmission of pleuropneumonia-like organisms is discussed. A husband and wife were cured with streptomycin. *G. M. Findlay*

2071. **Granuloma Inguinale and its Treatment with Oral Aureomycin**

M. ZISES and G. C. SMITH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 642–647, Nov., 1950. 15 refs.

Granuloma inguinale was first described by Conger and Daniels in 1896 as occurring amongst the negroes of British Guiana; since then reports have indicated that this troublesome condition is endemic throughout the entire southern United States. This paper concerns 17 negro patients from South Carolina, in smears from whose lesions donovania were demonstrated. They were treated with 25 g. of aureomycin, given in doses of 500 mg. 6-hourly for 12½ days. (In 3 cases slightly less than this amount was given and in 2 the treatment time was extended to 15 to 16 days.) Nausea with or without vomiting occurred in 8 cases. In 4 these symptoms were very slight, and they were minimized in the others by the ingestion of aluminium hydroxide. The follow-up period varied from 1 to 7 months. One relapse was noted 25 days after treatment: this patient was retreated

with the same dose and remained well 6 months later. One patient received a second course of aureomycin 1½ months after the first had been given, because the lesions had not completely healed, although no Donovan bodies could be demonstrated in the smears. The lesions healed and the patient was well when seen again a month later. *R. R. Willcox*

2072. **New Antibiotics (Streptomycin and Aureomycin) in Advanced Cases of Nicolas–Favre Disease.** (Essai des nouveaux anti-biotiques (streptomycine et auréomycine) dans les cas avancés de maladie de Nicolas–Favre)
J. LAMBILLON. *Annales de la Société Belge de Médecine Tropicale* [*Ann. Soc. belge Med. trop.*] **30**, 487–501, Sept. 30, 1950. 2 figs., 2 refs.

The results of sulphonamide and penicillin treatment in lymphogranuloma venereum were disappointing. Streptomycin, 1 g. daily for 4 to 6 months, was given in 4 cases in which there were bilateral inguinal buboes, the average total dose being 180 g. The action of streptomycin is very slow, but sure. In 2 cases, after streptomycin had been given for about one month, aureomycin was substituted with remarkable results. Aureomycin alone was then given in 7 long-standing cases with vaginitis, rectal stenosis, proctitis, and multiple fistulae. It was injected intramuscularly as a 1% solution in physiological saline. Injections containing 15 mg. were given once, twice, or even thrice daily. The results are said to have been remarkable, Total dosage was from 225 mg. to 3 g.
G. M. Findlay

2073. **Lymphogranuloma Venereum with Arthritis of the Hip-joint.** (Poroadenite inguinal com artrite da anca)
M. SAMPAIO and R. FARRAJOTA. *Trabalhos da Sociedade Portuguesa de Dermatologia e Venereologia* [*Trab. Soc. port. Derm. Vener.*] **8**, 222–223, Dec., 1950.

Lymphogranuloma venereum is a generalized infection and the virus may on occasion involve the joints. In a case with a large bubo in the left inguinal region there was pain on moving the left hip-joint. *X*-ray examination showed decalcification of the epiphysis of the femur and changes in the acetabulum. The patient was cured by three courses of sulphadiazine by mouth.
G. M. Findlay

2074. **Terramycin and Aureomycin in Rectal Stricture Due to Lymphogranuloma.** (Influência da terramicina e da aureomicina no aperto rectal de origem linfor-granulomatosa)
F. ANDRÊA. *Trabalhos da Sociedade Portuguesa de Dermatologia e Venereolgia* [*Trab. Soc. port. Derm. Vener.*] **8**, 238–240, Dec., 1950.

Four patients with stricture of the rectum and positive Frei tests were given terramycin or aureomycin every 6 hours. The terramycin was given for 7 days to a total of 100 capsules [? each of 250 mg.]. Both antibiotics caused remarkable improvement in the symptoms.
G. M. Findlay

SYPHILIS

2075. **Treatment of Early Syphilis, with Penicillin, Neoarsphenamine, and Bismuth, and with Penicillin and Bismuth alone**
F. J. G. JEFFERISS, R. R. WILLCOX, and G. L. M. MCELLIGOTT. *Lancet* [*Lancet*] **1**, 83–85, Jan. 13, 1951. 5 refs.

The difficult problem is discussed of assessing the merits of neoarsphenamine when combined with penicillin and bismuth in the treatment of early syphilis. Before the autumn of 1947, 561 patients were treated for primary and secondary syphilis with penicillin, neoarsphenamine, and bismuth. After that date, 183 similar cases were treated with penicillin and bismuth alone. The results of the two series are presented.

The first series consisted of 336 men and 225 women, of whom 145 had seronegative primary, 199 seropositive primary, and 217 secondary syphilis. Of these, the first 275 were given a total dose of 2·4 to 4 million units in 7½ to 12½ days and a course of neoarsphenamine and bismuth lasting from 6 to 10 weeks. One-third of the males and half the females were admitted to hospital and given 40,000 to 75,000 units of amorphous penicillin 3-hourly or 4-hourly for 7½ to 12½ days, while the rest were treated as out-patients with penicillin in oil–beeswax mixtures. The remaining 286 patients received 2·4 to 5 million units in 8 days (500,000 to 600,000 units in oil-wax daily) followed by 4·0 to 4·5 g. of neoarsphenamine (0·45 g. every 4 days) and 2·0 g. of bismuth (0·2 g. every 4 days). The toxic effects from bismuth and penicillin were unimportant, but those due to neoarsphenamine were comparatively numerous. These numbered 105, but this included 17 men and one woman with jaundice which the authors attribute to the virus of homologous serum hepatitis although the syringes and needles were boiled for 15 minutes. In all, 39 patients defaulted and 10 were reinfected. Among the remaining 512 cases there were 12 failures, 4 clinical and 6 serological relapses, and 2 doubtful neuro-failures. The successful 500 became sero-negative within a year.

The second series consisted of 123 men and 60 women, of whom 34 had sero-negative primary, 49 sero-positive primary, and 100 secondary syphilis. Of these patients 172 received 4·8 million units (double the dosage given in some cases in the earlier series) of penicillin in oil-beeswax mixtures in 8 daily injections of 600,000 units, followed by weekly or biweekly injections of 0·2 g. of bismuth oxychloride, 151 patients being given 1·5 to 2·5 g., and 32 less than 1·5 g. The remaining 11 patients received the same total dosage of penicillin and bismuth, but aqueous instead of oil–wax penicillin was injected 2-hourly. There were no adverse side-effects except a few cases of urticaria. In this series 55 patients defaulted in less than 3 months. The remainder (128) all became sero-negative within 12 months. The authors list 12 failures: 7 potential serological failures (5 defaulted within 10 months) and 5 potential clinical failures. These 5 patients all admitted re-exposure to infection and were probably reinfected, but the authors generously class 3 of them as relapses and only 2 as re-infections.

As only a little more than half of the total number of cases in both series were observed for 12 months or more, and as 7·5% of them defaulted while still seropositive, the authors do not attempt to calculate a percentage failure-rate. They think, however, that the end of the arsenical era may be at hand if penicillin-resistant strains do not appear. *T. Anwyl-Davies*

2076. **Bony and Periosteal Changes in Early Acquired Syphilis.** (Über Knochenund Periostveränderungen im Frühstadium der Lues acquisita)
K. SCHWARZKOPF and F. WESTERBURG. *Hautarzt* [*Hautarzt*] **1**, 515–517, Nov., 1950. 2 figs., 19 refs.

Foci of osteoperiostitis and small osteolytic processes are described in a patient with seropositive primary syphilis. The lesions were situated on the forehead and the left sternoclavicular joint. During the initial phases of antisyphilitic treatment a Herxheimer reaction occurred, and at the same time new foci appeared. Clinical cure was eventually obtained, but radiological evidence of bone involvement was still present some 2 weeks after the conclusion of treatment.
G. W. Csonka

2077. **Hepatitis associated with Syphilis and Treatment of Syphilis, with Special Reference to its Sequelae.** (Über die Hepatitis bei Lues und antiluischer Behandlung mit besonderer Berücksichtigung ihrer Folgekrankheiten)
L. BENDA, E. RISSEL, and H. THALER. *Deutsches Archiv für Klinische Medizin* [*Dtsch. Arch. klin. Med.*] **197**, 477–507, 1950. 11 figs., 42 refs.

Histological studies were carried out on 75 syphilitics with liver damage. Clinically the patients comprised cases of late (62) and early (7) jaundice after arsenotherapy, 3 cases of " icterus syphiliticus praecox ", and 3 of hepatitis without jaundice. Three of the early arsphenamine-jaundiced cases were distinct from the other 4 clinically and histologically, the jaundice being apparently obstructive in origin. In all other cases the histological picture was of the same type; details depended on the period of the illness at which the specimen was collected. The picture was that of a diffuse, chiefly central, zonal, necrotizing hepatitis which was essentially similar to that seen in infective hepatitis. Clear and careful descriptions are given in the text of the various stages, acute, regressive, and healing, of the process. The authors conclude that the late jaundice of arsphenamine therapy clinically and epidemiologically resembles that of homologous serum hepatitis and is probably caused by the same agent, whereas the early jaundice cases and those of icterus syphiliticus praecox are more closely related to infective hepatitis. They regard the antisyphilitic drugs as additional and accessory factors in the promotion of such hepatitis.

Nine patients treated with arsphenamine died in coma after becoming jaundiced. Necropsy revealed a picture also suggestive of death from virus hepatitis. Recovery either resulted in restitution of hepatic tissue or central and periportal sclerosis. Eleven cases of cirrhosis following arsphenamine jaundice were studied at various stages. Five had a history of alcoholic abuse, but in the others it appeared that the arsphenamine jaundice could be regarded as the forerunner of the cirrhosis.

[Those interested are advised to read the original.]
B. G. Maegraith

2078. **Results of Penicillin Treatment in Congenital Syphilis**
L. J. HANCHETT and M. E. PERRY. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **31**, 277–286, Nov., 1950. 1 fig., 6 refs.

This report concerns 142 previously untreated cases of congenital syphilis in patients ranging in age from 1 month to 31 years, who were treated in the case of infants with 100,000 to 600,000 units of penicillin per kg. body weight, and in the case of children over 11 and adults, with 2·4 to 8·0 mega units, given in individual doses of 15,000 to 50,000 units every 2 to 3 hours for 5 to 32 days. Of the 142, 75 were subsequently followed up for more than 2 years.

Of 37 patients under 2 years of age at the time of treatment, all were free of symptoms and serologically negative 2 years later and none had relapsed. On the other hand, of the 38 who were over 2 years of age, 91·3% were seropositive at 2 years, and 2 patients, both over 10 years of age, required re-treatment on account of a recurrence of interstitial keratitis. The first of these was successfully re-treated with penicillin, but the second, in spite of receiving a further 8 mega units of penicillin plus 33 hours of fever over 104° F. (40° C.), relapsed a second time 6 months later. Five patients had an abnormal spinal fluid before treatment, but when tested again 6 months to 2 years after treatment a normal fluid was found in 2 and a near-normal fluid (with a positive Kolmer reaction) in the remainder.
R. R. Willcox

2079. **The Effect of Previous Antisyphilitic Treatment on Present Treatment, as Indicated by the Records from the Nation-wide Study of Penicillin in Syphilis**
R. V. RIDER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 581–586, Nov., 1950. 5 figs.,

An attempt was made to determine, by the examination of existing records at the Central Statistical Unit at the Johns Hopkins University, Baltimore, whether treatment for syphilis with inadequate dosage makes subsequent treatment with standard dosage less effective. Graphs are presented of cumulative clinical and total failure rates among coloured and white patients treated with amorphous and crystalline penicillin, classified according to whether previous treatment had or had not been given. In the group treated with amorphous penicillin there were 1,056 negroes and 333 whites who had had previous treatment and 2,128 negroes and 671 whites who had not. Of those treated with crystalline penicillin G, 444 had had previous treatment and 1,828 had not. In the latter group no difference was noted between those previously treated and the others, the cumulative failure rate being in the region of 15% at 2 years and under 20% at 30 months. In those treated with amorphous penicillin,

however, there was a slight tendency for those treated for the second time not to do so well as those treated for the first time, the difference in cumulative failure rates amounting to 5 to 10% at 2 years. When the figure of those treated a second time was adjusted to include only those treated for the same syphilitic infection this difference became much more noticeable.

R. R. Willcox

2080. **A Clinical Psychometric Procedure in the Recognition of Early Dementing Paresis**

B. I. Lewis. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 534–553, Nov., 1950. 4 figs., 12 refs.

A psychometric procedure for the detection of mental deterioration in patients with neurosyphilis, and particularly of early simple dementing paresis, was applied to 72 patients. The Kohs block test and the Stanford–Binet vocabulary test were employed for this purpose. The results in cases of syphilis (1) without neurosyphilis, (2) with non-paretic neurosyphilis, (3) with paresis, and (4) with doubtful paresis are discussed. Evidence was obtained which suggests that the procedure indicates objectively the presence of mental deterioration and, roughly, its degree.

The procedure is simple and consumes little time, and is considered by the author to be of practical clinical value.

V. E. Lloyd

2081. **Investigations of Psychological Processes in Patients with Neurosyphilis**

T. H. Sternberg and M. C. Zimmerman. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 519–533, Nov., 1950. 4 figs., 19 refs.

The Wechsler–Bellevue adult intelligence test was used in a study of psychological processes in 66 patients with neurosyphilis. The purpose of the study was to evaluate the use of such tests in active neurosyphilis and to clarify such questions as the possibility of psychological correlates of specific pathological changes and the value of psychological tests in the preliminary study of the patient, as a prognostic aid, and as a measure of therapeutic efficacy. The group studied included cases of syphilis without neurosyphilis, of active asymptomatic neurosyphilis, of inactive neurosyphilis, of active symptomatic neurosyphilis, of tabes dorsalis, and of psychosis.

On average, patients with early and latent syphilis without neurosyphilis were found to be of normal intelligence; those with inactive neurosyphilis were of borderline to dull normal intelligence; those with active symptomatic neurosyphilis were of a dull normal level; and those with active asymptomatic neurosyphilis were assessed at the borderline level of intelligence.

[This is a preliminary report of an investigation in which the authors plan to use a battery of 8 intelligence tests for the same purpose. The full report of the completed study may well reveal greater differences between the various types of neurosyphilis.]

V. E. Lloyd

2082 (*a*). **Cerebral Blood Flow and Oxygen Consumption in Neurosyphilis**

J. L. Patterson, A. Heyman, and F. T. Nichols. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1327–1334, Oct., 1950. 4 figs., 12 refs.

It would seem obvious that the narrowing of the lumen of the cerebral vessels which occurs in meningovascular neurosyphilis and general paralysis must lead to a decrease in the flow of blood through these vessels as compared with normal subjects. In the experiments described in this paper cerebral blood flow was determined by the nitrous oxide technique of Kety and Schmidt (*J. clin. Invest.*, 1948, **27**, 476) in 26 patients with general paralysis, 9 with meningovascular syphilis, and 23 with asymptomatic neurosyphilis, and in a control group of 16 non-syphilitic patients. The cerebral oxygen consumption was estimated from the product of the cerebral blood flow and the difference in oxygen content between arterial and venous blood.

In the group of patients with meningovascular syphilis the cerebral blood flow was, on the average, only 66% of normal, but there was no correlation between the reduction in blood flow in particular cases and the severity of the clinical symptoms. There was also a diminished oxygen consumption (77% of that of the normal group).

In patients with general paralysis the cerebral blood flow was reduced to 72% of normal, and a corresponding diminution in oxygen consumption was found. In some patients with general paralysis the oxygen consumption was extremely low—in one case only 24% of normal—and there was a definite relationship between the degree of dementia and the reduction in oxygen consumption. Any improvement in the mental state after treatment with penicillin or pyrexia was accompanied by an increase in cerebral oxygen consumption. In patients with asymptomatic neurosyphilis normal values were obtained for both cerebral blood flow and oxygen consumption.

Ruby O. Stern

2082 (*b*). **The Effects of Induced Fever on Cerebral Functions in Neurosyphilis**

A. Heyman, J. L. Patterson, and F. T. Nichols. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1335–1341, Oct., 1950. 4 figs., 13 refs.

Of the patients referred to in the previous paper (see Abstract 2082 (*a*)) 14 with general paralysis and 13 with asymptomatic neurosyphilis were treated with induced pyrexia, 2 being inoculated with malaria parasites, and the remainder given an intravenous injection of 0·1 ml. of a suspension of heat-killed typhoid bacilli. The maximum temperature ranged from 101° to 104° F. (38·3° to 40° C.). The cerebral blood flow was determined when the temperature was normal and again at the height of the fever. In the patients with asymptomatic neurosyphilis values for both cerebral blood flow and cerebral oxygen consumption were normal when afebrile and showed only very slight variations during the febrile period. In those with general paralysis cerebral blood flow and oxygen consumption were abnormally low when afebrile, but increased during the

period of the fever by 30% and 24% respectively. The authors suggest that the good effects of pyrexial therapy in general paralysis are due, at least in part, to dilatation of the cerebral vessels and the subsequent increase in cerebral blood flow. *Ruby O. Stern*

2083. **Neurosyphilis IV. Posttreatment Evaluation Four to Five Years following Penicillin and Penicillin plus Malaria**
A. C. CURTIS, W. T. KRUSE, and D. H. NORTON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 554–565, Nov., 1950. 10 figs., 8 refs.

A total of 639 patients with neurosyphilis have been treated during the 5 years since the introduction of penicillin therapy at the University Hospital, Ann Arbor, Michigan. A report is now issued on its effect on 430 of these patients who have been adequately observed. One-half of the number were treated with penicillin and malaria, and one-half with penicillin alone, and 30% of the patients have been observed over a period of 4 to 5 years. The series includes cases of meningovascular syphilis, asymptomatic neurosyphilis, paresis, and tabes dorsalis, with a preponderance of the last two types. Penicillin therapy consisted of a total dose of 4,000,000 units, given over 12½ days; malaria therapy consisted of 50 or more hours of fever above 103·5° F. (39·7° C.).

Details of the type and degree of improvement observed in the cerebrospinal fluid (C.S.F.) are set out in graphic form. The cell count and protein content, when increased, returned to normal figures within 3 to 9 months. The colloidal gold reaction became normal in 18 to 36 months. The Kahn test, however, remained positive in many instances for a longer period, and at the end of 4 to 5 years only 40% of patients had achieved a negative result. In general the attainment of a normal C.S.F. was not necessarily related to clinical recovery. There appeared to be little difference between the efficacy of penicillin with and without malaria except in the group of paretics, in which penicillin–malaria therapy gave superior results.

Necropsy observations on the brain were made in 4 cases [type of neurosyphilis not stated]. In 2 patients who died during treatment ample evidence of active neurosyphilis was found. Two patients died 2 years after treatment, and the brain in these cases showed little or no histological evidence of neurosyphilis.

The authors conclude that penicillin alone is adequate for all types of neurosyphilis except, possibly, severe paresis and primary optic atrophy. *V. E. Lloyd*

2084. **Studies on Increasing the Sensitivity of the Treponemal Immobilization Test for Syphilis**
F. A. THOMPSON and H. J. MAGNUSON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 21–34, Jan., 1951. 4 refs.

The treponemal immobilization test described by Nelson and Mayer (*J. exp. Med.*, 1949, **89**, 369) has been made more sensitive by increasing the final concentration of guinea-pig serum from 5·6 to 22·2%. It is suggested that the immobilization test can be rendered even more sensitive by increasing at the same time the final concentration of the patient's inactivated serum from 11·1 to 22·2%. The reliability and significance of the test still need further evaluation. *G. M. Findlay*

2085. **Skin Testing with a Purified Suspension of *Treponema pallidum***
L. C. MARSHAK and S. ROTHMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 35–41, Jan., 1951. 3 figs., 19 refs.

Rabbit's testicles infected with the Nichols strain of *Treponema pallidum* were used to prepare a suspension of treponemata which was treated with 0·1% formalin. An intradermal injection of 0·1 ml. was made into the flexor surface of one forearm, while into the corresponding area of the other arm was injected the same amount of a suspension from normal rabbit testicles. Normal persons and those with secondary syphilis gave negative results, but in those with tertiary or congenital syphilis there was a tuberculin-like reaction. The term " treponemin test " is suggested for this reaction.
G. M. Findlay

2086. **Bismuth Penicillin in the Treatment of Acute Syphilitic Orchitis of Rabbits**
S. MONASH and J. A. KOLMER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 689–693, Nov., 1950. 8 refs.

Bismuth penicillin is a whitish, crystalline substance consisting of 3 molecules of penicillin combined with one atom of tervalent bismuth; its correct chemical name is therefore bismuth tripenicillinate (or tripenicillate). Its molecular weight is approximately 1,209 and it has a theoretical bismuth content of 17·29%. The preparation used by the authors was a suspension in 2% aluminium monostearate gelled in sesame oil, and contained 0·255 mg. of bismuth per 1,000 units of penicillin. For clinical trials it is suggested that doses of 400,000 to 600,000 units, containing approximately 0·1 to 0·15 g. of bismuth, be used.

Rabbits were inoculated intra-testicularly with the Nichols–Hough strain of *Treponema pallidum*, and treatment was instituted 6 weeks later in those which had acquired a dark-field-positive orchitis. Dark-field examinations were later made on 11 occasions at intervals ranging from 1 to 70 days after treatment, at which time lymph-node transfer was made into fresh rabbits which were observed for a further 4 months. Ten rabbits were given single graded doses of 5,000 to 100,000 units of bismuth penicillin per kg. body weight, and the minimum curative dose was found to be in the region of 5,000 units per kg., while in a similar series treated with a single dose of sodium penicillin G in oil and wax the minimum curative dose was 10,000 units per kg. Two further groups, each of 10 rabbits, were treated with the two preparations, this time 800 to 16,000 units per kg. being given in 8 daily injections. With penicillin in oil and wax the minimum curative dose was approximately 8,000 units per kg., but with bismuth penicillin it was reduced to 4,000 units per kg. *R. R. Willcox*

Disorders of the Genito-urinary System

2087. **Purpura of the Urinary Tract, Focal Nephritis, and Bright's Disease.** (Purpura der Harnwege, Herdnephritis und Morbus Bright)
G. W. GUNTHER. *Zeitschrift für Urologie* [*Z. Urol.*] **43**, 496–520, 1950. 13 figs., 40 refs.

In asking whether essential renal haematuria exists, the author makes a distinction between visible haematuria and the microscopical finding of blood associated with renal casts (erythruria). The latter may be, and frequently is, renal in origin (as in focal nephritis), but the latter, he contends, is not truly renal but derives from haemorrhages in the calyces and pelvis (often from haemorrhagic pyelitis). In a critical survey of histopathological reports he describes a case of Schönlein's purpura with massive haematuria in a boy of 9, and cites an instance of polyarteritis nodosa with haematuria in which haemorrhagic infiltration of the renal pelves and calyces proved to be the source of the bleeding (without any changes such as small infarcts in the kidney proper). In cases of malignant hypertension any associated haematuria may be ascribable to petechiae in the pelvis, and similar lesions may be met with in trench nephritis.
J. D. Fergusson

2088. **Terramycin in Urinary Tract Infections**
R. G. DOUGLAS, T. L. BALL, and I. F. DAVIS. *California Medicine* [*Calif. Med.*] **73**, 463–465, Dec., 1950.

Urinary tract infections in 32 women with obstetrical or gynaecological conditions were treated with terramycin. Results were classified as " good " if the patient was afebrile and symptomless and the urine pus-free and sterile within 72 hours of starting treatment, " equivocal " if more than 72 hours was required or bacilluria with minor symptoms persisted, and " poor " if the course of the infection was unaltered. Of 27 cases without obstructive or other predisposing renal-tract lesions, results were good in 24 and equivocal in 3; of 5 with such lesions, they were good in 2, equivocal in 1, and poor in 2. Good results were obtained in 19 out of 20 infections due to *Bacterium coli* or *Aerobacter aerogenes*, but in only 1 out of 4 due to *Pseudomonas aeruginosa* (the other infections were due to: *Proteus vulgaris*, 1; *Staphylococcus albus*, 2; aerobic diphtheroids, 3; aerobic non-haemolytic streptococci, 2). Sensitivity tests were carried out *in vitro* on 40 organisms isolated from urine; only 2 out of 20 strains of *Bact. coli* and *A. aerogenes* were resistant to 50 μg. per ml. of terramycin, as compared with 9 out of 18 strains of *Ps. aeruginosa*. Comparative tests on 19 organisms showed no gross disparity between individual sensitivities to aureomycin, chloramphenicol, and terramycin. The authors give no details of the doses of terramycin used in the present investigation, but suggest the following schemes: (1) for uncomplicated cases infected with *Bact. coli* or *A. aerogenes*, 250 mg. 6-hourly for 5 days, then twice daily for 5 days; (2) for cases infected with *P. vulgaris* or *Ps. aeruginosa* or having other urinary-tract lesions, 500 mg. 6-hourly for 5 days, then 250 mg. 6-hourly for 5 days.

[It seems scarcely justifiable to base a recommendation for the treatment of *P. vulgaris* infections on experience with a single case.] *H. McC. Giles*

2089. **Relation of Creatinine to Nonprotein Nitrogen in Azotemic States**
P. GABERMAN, D. H. ATLAS, E. M. KAMMERLING, L. EHRLICH, and J. ISAACS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1246–1249, Dec. 9, 1950. 3 figs., 13 refs.

The authors consider the term " extrarenal azotaemia " to be unspecific in that it covers a variety of conditions which differ in their pathogenesis. Although much has been written on the subject, there are very few references to creatinine metabolism in azotemic states. The authors therefore set out to investigate this aspect of the problem in three types of azotaemia—extrarenal (22 cases with 12 deaths and 8 necropsies), primary renal (15 cases), and postrenal or obstructive (7 cases). The estimation of blood non-protein nitrogen (N.P.N.), urea nitrogen, and creatinine levels in these cases showed that there was a linear correlation between the N.P.N. and urea levels in all three categories. On the other hand, there was no diagnostically significant correlation between blood creatinine and N.P.N. levels in any of the categories studied; but although the former might be increased in proportion to the increase in the latter in cases of any type, a disproportionately low creatinine level as compared with the rise in N.P.N. level would usually appear to indicate azotaemia of extrarenal or postrenal origin.
D. Preiskel

2090. **Treatment of Potassium Retention in Anuria with Cation Exchange Resin. A Preliminary Report**
J. R. ELKINTON, J. K. CLARK, R. D. SQUIRES, L. W. BLUEMLE, and A. P. CROSLEY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 547–552, Nov., 1950. 3 figs., 23 refs.

The ammonium form of a carboxylic cation-exchange resin was administered in daily doses of 50 g. by mouth or retention enema to 3 patients with a high serum potassium concentration due to severe renal disease. In all 3 the serum potassium concentration was reduced to normal levels. In one patient there occurred an excessive parallel removal of sodium, which was replaced by feeding sodium bicarbonate. Administration by retention enema appeared to be as effective as by mouth and was more convenient in that the resin could be collected after use and its cation content estimated.

[The difficulty of sodium removal could be avoided by the use of a mixture of the ammonium and the sodium forms rather than the ammonium form of the resin alone.] *G. M. Bull*

Disorders of the Locomotor and Osseous Systems

2091. **Some Examples of the Indications for Parathyroidectomy, Particularly in Chronic Rheumatism.** (Documents pour servir aux indications de la parathyroïdectomie. (En particulier dans les rhumatismes chroniques))

P. MALLET-GUY and P. GUIGOU. *Journal de Médecine de Lyon* [*J. Méd. Lyon*] **31**, 991–1000, Dec. 5, 1950.

The authors of this article describe a number of cases of neurofibromatosis, scleroderma, spinal osteomalacia, and chronic back pain due to spondylitis in which removal of the parathyroid gland on one side gave relief—in one case in which the operation was performed under local analgesia the pain vanished as the gland was removed. [They do not distinguish between osteoporosis and osteomalacia and the rationale of the operation is not discussed.] Three conditions which must be fulfilled to obtain success in cases of chronic rheumatism are that the tissue removed be shown to be parathyroid by histological examination, that there be hypercalcaemia, and that the rheumatism be confined to the spine.

G. S. Crockett

2092. **Objective Assessment of Improvement in Rheumatoid Arthritis**

O. JANUS. *British Medical Journal* [*Brit. med. J.*] **2**, 1244–1249, Dec. 2, 1950. 6 figs., 12 refs.

The introduction of the potent antirheumatic agents, cortisone and adrenocorticotrophin (ACTH), has underlined the need for reliable objective tests of improvement in rheumatoid arthritis, sensitive and accurate enough to demonstrate a response to single injections of cortisone or ACTH, which would be used in estimating dosage and in comparing the effects of unknown substances, standard active preparations, and inert controls in the same patient, and which would eliminate the psychological factors involved in any subjective or clinical assessment. By measurements of joint tenderness, strength of grip, articular blood flow, finger-tip temperature, and number of circulating eosinophils in cases of rheumatoid arthritis under standard conditions, the author claims to have evolved a reliable method of objective assessment responsive to the effects of single doses of cortisone and ACTH. A new method for measuring joint tenderness in the fingers is described, and both this measurement and the measurement of grip are reproducible within a narrow range. Blood flow in involved knee-joints is measured by plethysmography, and skin temperature by thermocouples on the finger-tips. Daily measurements were carried out on patients at rest under basic conditions and those in whom all readings showed steady improvement, indicating that they were going into remission on rest alone, were eliminated, only those patients whose measurements were largely unchanged over a period of several days being selected for study of the effects of treatment. After an injection of 25 mg. of ACTH a lessening of joint tenderness and an increase in strength of grip, maximal between 6 and 8 hours, and a fall in the number of circulating eosinophils were demonstrated. Knee blood flow showed a biphasic response, a variable initial increase at 6 hours being followed by a rapid decrease between 8 and 12 hours after the injection. Skin temperature was unchanged. The responses to a single injection of 200 mg. of cortisone were similar but slower, except that there was not the early increase in knee blood flow which was produced by ACTH. In view of this variability in response, it was decided that the measurement of knee blood flow was not suitable for inclusion in the test.

In a number of experiments, single injections of ACTH (in 3 different test doses), of cortisone, and of an ACTH peptide produced regular and statistically significant deviations in eosinophil count, pain threshold for joints, and strength of grip, whereas no such deviations were seen after the administration of various other drugs which have been claimed to be effective in rheumatoid arthritis, or after injections of inert substances. It was noted, however, that of 10 patients tested there appeared to be some response to aspirin in 3, in all of whom the drug produced eosinopenia; the eosinophil count was unchanged in the remaining 7 cases. *Ellis Dresner*

2093. **The Manubrio-sternal Joint in Rheumatoid Arthritis**

A. BOGDAN and J. CLARK. *British Medical Journal* [*Brit. med. J.*] **2**, 1361–1362, Dec. 16, 1950. 5 figs., 5 refs.

A report is presented, from the Westminster Hospital Rheumatism Unit, of 5 cases of involvement of the cartilaginous manubrio-sternal joint in rheumatoid arthritis. Pain, swelling, and tenderness at the joint site were noted, and were aggravated by respiratory movements—particularly coughing, sneezing, and yawning. Differential diagnosis had to be made from angina in one case in which the pain was particularly aggravated by the deeper inspirations resulting from exertion. In one case the affection of this joint was the first manifestation of rheumatoid arthritis. Radiological changes are best seen in coned lateral views (of which four examples are reproduced) and occur later; they may include irregularity and narrowing of the joint space, erosion of the articular surfaces, and irregular expansion of the articulating bone ends. Progression to bony ankylosis was not observed in these cases. *Harry Coke*

2094. **The Frequency of Fatty Herniae with Necrotic Lesions as a Cause of Lumbago.** (La frecuencia de hernias grasas con lesiones necróticas como causa de lumbago)

H. DAL LAGO and R. A. VERA. *Revista de Ortopedia y Traumatología* [*Rev. Ortop. Traum.*] **20**, 160–164, Oct., 1950. 4 figs.

Neurology

2095. **Clinical Correlates of Exceedingly Fast Activity in the Electroencephalogram**
E. L. GIBBS, F. M. LORIMER, and F. A. GIBBS. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **11**, 323–326, Nov., 1950. 2 figs.

Bursts or runs of 30 to 40 per second activity with a voltage of more than 15 microvolts are not encountered in the electroencephalograms of normal control subjects. A study of 68 patients with this type of electroencephalographic disorder reveals that it is most likely to appear during drowsiness and very light sleep. The most common symptoms of patients with such disorder are: headaches, " blackout " spells, restlessness, personality changes, paresthesias, and vertigo. These patients do not fit into any recognized clinical diagnostic group, but they usually fit the characterization " dull psychopath ". No common etiological factor could be found, but by analogy with other types of cerebral dysrhythmia it is believed that exceedingly fast activity is an irritative reaction to an intermediate degree of brain injury of a non-specific type.—[Authors' summary.]

2096. **The Use of Sedative-induced Sleep as an Aid to Electroencephalographic Diagnosis in Children**
P. KELLAWAY. *Journal of Pediatrics* [*J. Pediat.*] **37**, 862–877, Dec., 1950. 12 figs., 35 refs.

The use of pentobarbitone (" nembutal ") as a means of inducing sleep before electroencephalography in a series of 400 possibly epileptic children is described, pentobarbitone being chosen because, in correct dosage, it does not of itself alter the pattern greatly and because it is not so anticonvulsant as to mask epileptic activity. A dose of 0·75 gr. (48 mg.) was given to those aged 3 to 10, and 1 to 1·5 gr. (65 to 100 mg.) to those aged 11 to 14. In a high proportion of cases abnormal discharges were recorded during sleep thus induced, these being either focal in type or of a generalized wave-and-spike pattern. In some of these cases there had previously been failure to evoke abnormalities by hyperpnoea or by the injection of leptazol, and in some the discharge was shown to be focal, although routine recordings had revealed only generalized abnormalities. Experience is sometimes necessary in distinguishing the epileptic discharge from the normal high-amplitude sleep activity, but this method of examination is always valuable and is sometimes indispensable to diagnosis. [A selection of excellent recordings is reproduced.] *D. P. Jones*

2097. **The Effect of Adrenocorticotropic Hormone in Epilepsy**
R. KLEIN and S. LIVINGSTON. *Journal of Pediatrics* [*J. Pediat.*] **37**, 733–742, Nov., 1950. 5 figs., 7 refs.

A series of 6 epileptic children aged 4 to 13 years were treated with adrenocorticotrophin (ACTH) in doses of 40 to 100 mg. daily. Four of them showed improvement objectively. On the electroencephalogram, slow spike-and-wave forms, abnormally fast activity, and abnormally slow waves disappeared. One patient with petit mal showed no improvement. Two patients were given short courses of deoxycortone acetate, and in one of these there was clinical and encephalographic improvement. One patient was given cortisone, 100 mg. daily for 7 days; there was a temporary diminution in the number of seizures, but marked personality changes were induced. The authors consider that the beneficial action of adrenal hormones in epilepsy is due to their effect on carbohydrate, protein, and fat metabolism.
J. Vernon Braithwaite

2098. **A Study of Epilepsy in its Clinical, Social and Genetic Aspects.** [In English]
C. H. ALSTROM. *Acta Psychiatrica et Neurologica* [*Acta psychiat., Kbh.*] Suppl. 63, 1–284, 1950. 7 figs., bibliography.

2099. **Abdominal Epilepsy.** (Epilepsie abdominale)
M. T. MOORE. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1352–1356, Dec. 23, 1950. 37 refs.

2100. **The Treatment of Migraine and Intractable Headache with Aerosols of Ergotamine Tartrate and of Procaine.** (Traitement des migraines et des céphalées rebelles par les aérosols de tartrate d'ergotamine et de novocaine)
J. TABART. *Presse Médicale* [*Pr. méd.*] **58**, 1351–1352, Dec. 2, 1950. 2 refs.

Patients with migraine or other intractable headaches resistant to the usual therapeutic procedures were given aerosols of procaine (50 to 100 mg.) or ergotamine tartrate (0·25 to 1 mg.), repeated at intervals. With either drug, remissions—often prolonged—were induced in 25 out of 41 cases of migraine and in 9 out of 12 patients with non-migrainous headache. Ergotamine tartrate appeared to be more effective administered in this way then when it was given orally.
G. Ansell

2101. **Myasthenia Gravis associated with Adrenocortical Insufficiency. Report of a Case with Post-mortem Findings and a Review of the Literature**
C. A. KANE and L. WEED. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 939–944, Dec. 14, 1950. 3 figs., 24 refs.

Addison's disease and myasthenia gravis developed simultaneously in a male aged 18 years. The patient gave a history of generalized weakness, double vision, ptosis, slurred speech, and dysphagia. Nasal regurgitation of liquids had also occurred. During the few weeks before his admission to hospital the patient suffered from anorexia, nausea and vomiting, and constipation. On

admission he was found to be a tall, asthenic youth with drooping eyelids and an open mouth. His voice had a nasal twang. Bronzing of the skin was observed, especially in the lumbo-dorsal region. In addition, there were numerous pigmented naevi. Examination of the eyes showed the presence of bilateral ptosis. The musculature was hypotonic, and dynamometer tests gave a poor response. He could not sit up unaided. Quick movements soon produced fatigue. Neostigmine tests confirmed the diagnosis of myasthenia gravis. The systolic blood pressure was 76 mm. Hg and the diastolic pressure was 60 mm. Hg. The blood urea level was 45 mg. per 100 ml. and blood sugar level 69 mg. per 100 ml. Serum content of chloride, sodium, and potassium was found to be 88·0, 128·7, and 6·7, respectively, in milliequivalents per litre. The Robinson–Powers–Kepler water test was positive. Thorn's adrenocorticotrophic test showed no response. A 17-ketosteroid assay revealed urinary excretion of less than 1 mg. in 24 hours.

The patient's condition improved with neostigmine and deoxycortone administration, but a relapse occurred about 2 months after his discharge from hospital and death took place after an acute attack of dyspnoea and cyanosis. An enlarged thymus was found at necropsy, the gland weighing 45 g. A focus of lymphocytic infiltration was detected in the psoas muscle. Both adrenal glands showed pronounced cortical atrophy. The pituitary gland contained hyperplastic chromophobe cells, but acidophil cells were few in number and basophil cells were rarely encountered. *A. Garland*

See also Section Pathology, Abstract 1885.

CENTRAL NERVOUS SYSTEM

2102. **Early Diagnosis of Subacute Combined Degeneration of the Cord. Value of Gastric Biopsy**
R. K. Doig, R. Motteram, E. G. Robertson, and I. J. Wood. *Lancet* [*Lancet*] **2**, 836–841, Dec. 23, 1950. 8 figs., 8 refs.

The authors of this paper emanating from the Royal Melbourne Hospital stress the importance of early diagnosis of subacute combined cord degeneration if treatment is to be wholly successful. Cases are often missed either because limb dysaesthesiae are neglected or because of reluctance to diagnose the condition unless a well-defined pernicious-anaemia blood picture is present.

Gastric biopsy with a flexible gastric-biopsy tube was undertaken in selected cases. Fragments of mucosa 1 mm. in diameter and extending down to the muscularis were removed for section. The histological features are described and photomicrographs are reproduced. The changes described are not specific, but were seen in all of 26 cases of pernicious anaemia and in only 2 of 278 dyspeptics who did not have pernicious anaemia. In cases of histamine-fast achlorhydria, such as those due to alcohol, unassociated with pernicious anaemia, the findings are different. The authors believe that in all cases of subacute combined degeneration there is histamine-fast achlorhydria, and if a microcytic anaemia be present it is due to causes other than the primary disease.

The first case described was one in which peripheral neuritis appeared to be the clinical diagnosis and the neurological symptoms were grossly in excess of the signs. The peripheral-blood and bone-marrow pictures were normal—probably because the patient had had liver therapy although no blood count had been done. The second case was one of alcoholic peripheral neuritis with a histamine-fast achlorhydria which had incorrectly been diagnosed as suspected subacute combined degeneration. In the third patient positive neurological signs were not present even 2 years after the onset of symptoms, and, because of normal blood findings, the diagnosis was not made until he developed a gross paraplegia. Had gastric biopsy been undertaken earlier, then probably the diagnosis would have been made before the development of irrecoverable cord damage. The fourth case illustrates the problem of the patient who has been given liver therapy without adequate blood investigation and later develops neurological signs. Should the dosage be increased under the assumption that the diagnosis is correct or should therapy be discontinued in an attempt to prove the diagnosis but with the risk of severe cord damage? In this case, gastric biopsy supplied the answer. The fifth case is very interesting because the cord signs developed rapidly in 2 weeks in a previously healthy woman. Although there was no macrocytosis of the peripheral blood there was an increase in the mean erythrocyte volume and the bone marrow was very suggestive of pernicious anaemia. Gastric biopsy confirmed the diagnosis.

[The paper is a valuable one. The authors do not advocate gastric biopsy as a routine in suspected cases of subacute combined degeneration, but its use in cases similar to those described above. If confined to such cases, the investigation may prove of great value. Let us hope that it will not be abused.] *M. H. Pappworth*

2103. **Thrombotic "Hydrocephalus" in Insulin Therapy**
J. Donnelly and E. J. Radley-Smith. *Lancet* [*Lancet*] **2**, 904–909, Dec. 30, 1950. 27 refs.

The authors prefer this term "thrombotic 'hydrocephalus'" for the condition of increased intracranial pressure consequent on thrombosis of the superior longitudinal sinus, although they point out that the increase in the amount of cerebrospinal fluid (C.S.F.) must be only slight in view of the normal findings on ventriculography or encephalography in such cases and the relief of symptoms after withdrawal of comparatively small amounts of C.S.F. They report 3 cases in patients who, during the course of combined insulin and electroconvulsive therapy, developed signs suggesting increased intracranial pressure associated with relatively few other neurological signs. The C.S.F. in each case was normal, though under increased pressure, and ventriculograms in 2 of the cases were normal. They were treated by repeated lumbar puncture and made an uneventful recovery, though in each case there were slight residual signs.

In discussing the possible causes of the thrombosis, the authors point out that an epileptic fit, by increasing intrathoracic and intra-abdominal pressure, will cause a rise in the venous pressure within the skull and may thereby cause damage to the vessel wall resulting in mural thrombosis. On the other hand, the profuse fluid loss during hypoglycaemia may lead to an increased tendency for the blood to clot, and they suggest that some of the deaths hitherto attributed to " hypoglycaemic encephalopathy " are in reality due to thrombotic " hydrocephalus ".

[This paper does not really advance our knowledge of this interesting, but still somewhat obscure, condition. It is unfortunate that in the cases described the authors did not carry out phlebography to determine whether in fact the cerebral veins or sinuses were obstructed.]

N. S. Alcock

2104. **Supranuclear Bulbar Palsy (Pseudobulbar Palsy) in Mitral Stenosis**

K. W. G. Heathfield and E. C. O. Jewesbury. *British Medical Journal* [*Brit. med. J.*] **2**, 1196–1198, Nov. 25, 1950. 10 refs.

Three unusual cases are described of supranuclear bulbar palsy developing, in young people suffering from mitral stenosis, as a result of bilateral cerebral emboli. The prospects of improvement in these cases are considered to be better than in most cases of supranuclear bulbar palsy resulting from bilateral cerebral thromboses, since diffuse arteriosclerotic changes are not present in the younger patients. The authors make a plea for the use of the term " supranuclear bulbar palsy " rather than the unsatisfactory, and to some extent meaningless, name of " pseudo-bulbar palsy " which is in general use.

J. W. Aldren Turner

2105. **Rare Forms of Paroxysmal Trigeminal Neuralgia, and their Relation to Disseminated Sclerosis**

W. Harris. *British Medical Journal* [*Brit. med. J.*] **2**, 1015–1019, Nov. 4, 1950. 7 refs.

Several problems concerning facial pain are considered in this article. The author describes 5 cases in which there was a sudden onset of numbness of one side of the face with complete anaesthesia of the whole of that side of the face and tongue; in a year or less the numbness had disappeared and the patient remained well until the development of paroxysmal trigeminal neuralgia without sensory impairment some years later. The trigeminal neuralgia has been cured by injection of the Gasserian ganglion in all 5. One of these patients developed disseminated sclerosis 11 years after the onset of the trigeminal neuralgia, but the other 4 have shown no sign of this disease. The author discusses the question whether disseminated sclerosis could have been the essential cause of this unusual clinical picture; he concludes that this is most unlikely, and that a patch of neuritis on the root of the fifth nerve at its junction with the pons was the probable basic pathology.

Attention is drawn to the rare cases in which analgesia of the third division cannot be obtained by injection of the Gasserian ganglion, and two examples are cited in which subsequent sensory-root section also failed to produce sensory impairment in the third division. The author also discusses briefly the facial pain and paraesthesiae which may occur following a medullary thrombosis, and describes an unusual case in which typical paroxysmal neuralgia was confined to the supraorbital region for 23 years before there was any spread to the maxillary distribution.

J. W. Aldren Turner

2106. **On the Detection of Intracranial Pathology by Ultrasound**

H. T. Ballantine, R. H. Bolt, T. F. Hueter, and G. D. Ludwig. *Science* [*Science*] **112**, 525–528, Nov. 3, 1950. 4 figs., 8 refs.

When a beam of " ultrasound " passes through the tissues the strength of the received signal on the other side is reduced by refraction and scattering, but is mainly dependent on absorption and reflexion at interfaces. These depend on the varying physical properties of the tissues concerned, and the differences in attenuation by fluid and brain are such that the possibility of ultrasonic ventriculography, or even of the recognition of some intracranial tumours as such, exists. Frequencies between 800 kc. and 2·5 Mc., generated by a crystal oscillator, have been used in preliminary work. It has been found that an intensity of about 1 watt per sq. cm. seems to give adequate transmission, and to be free from the risk of causing pain or tissue necrosis.

On the results of simple line-scans the authors feel able to state that ventriculograms can be obtained [though it is clear that further work will be necessary before the method yields clinically useful results].

W. A. Cobb

2107. **Experimental Study of a Case of Insensitivity to Pain**

G. A. McMurray. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 650–667, Nov., 1950. 5 figs., 18 refs.

Investigations are described on a healthy subject, aged 22, whose medical history, known since she was 21 months old, showed that she had apparently always been indifferent to painful stimuli, being unaware of cuts and burns, etc. Psychological and neurological examinations were negative, apart from absent corneal reflexes. A pinprick was readily felt, but there was no element of pain in the sensation. Tickle sense and itching were also absent. The formal investigations consisted of the application of painful stimuli (iced water, hot water, and electrical stimulation of the skin), and the assessment of whether pain was felt or not was made by means of: (1) verbal report by the subject; (2) wincing or other overt reaction; and (3) physiological responses normally accompanying the sensation of pain, such as alterations in blood pressure, pulse rate, and respiration. In no test was the sensation of pain made apparent. A skin biopsy was performed and the material, stained supravitally, showed that the peripheral innervation did not differ from the normal. The article includes a short review and discussion of previously reported cases.

J. B. Stanton

Psychiatry

2108. **Human Relationships in Tuberculosis**
J. HARTZ. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 1292–1305, Oct. 6, 1950.

This is a review, with illustrative cases, of the various types of emotional reaction found in patients with tuberculosis, their influence on the course of the disease, and their relevance to treatment.

The attitude of the patient is of first importance. The layman commonly regards tuberculosis with awe, and even in doctors the reaction may be one of irrational fear. Some patients interpret the advent of tuberculosis as a punishment for sin; others appear stunned. A phase of mild depression, lasting for a few weeks, is probably the usual response; this is replaced by an acceptance of the disease, and later by a semblance of cheerfulness. Persistence of depression for more than 2 months is a bad sign. Beneath the mask of cheerfulness there is as a rule a great deal of anxiety.

The patient's personal history, if it is skilfully taken, should provide clues to potentially harmful attitudes. The author estimates that about one-third of tuberculous patients have emotional problems serious enough to cause difficulty in treatment. The patient may, for example, be convinced that the diagnosis is incorrect and, leaving the hospital, plunge directly into full-time work, so that he falls ill again; this tends to occur in rigid, egocentric people. Another may do very well in hospital, but develop a complication on the eve of his departure, not once, but several times. To such people hospital is a refuge from some intolerable situation. Some very passive individuals give up trying to get well and sink into chronic invalidism.

A cardinal problem for the tuberculosis patient is that of accepting the dependent role which the disease exacts without undue guilt or anxiety. To certain people the idea of dependence seems dangerous or degrading, and they may struggle against the acceptance of care from others. Tuberculosis is viewed, by a minority of its victims, as a gradual suicide; the wish to die is implied by their actions, or even explicitly stated. In a few, the illness guarantees the care and affection necessary for their psychic equilibrium, and discharge from hospital may precipitate a psychosis.

There is a need for caution in applying psychotherapy, since an interview which arouses strong emotion may be followed by an increase or recrudescence of toxic symptoms. The timing of psychotherapeutic procedures must therefore be judged with care.

This paper also contains the report of a severely neurotic patient with progressive tuberculosis who was given intensive psychotherapy over about 2 months. Improvement in the mental condition was attended by arrest of the disease and eventual recovery. In this patient psychiatric treatment was clearly a life-saving measure. *Desmond O'Neill*

2109. **Studies of Palmar Hand Sweat in Healthy Subjects and in Patients with Neurocirculatory Asthenia (Anxiety Neurosis, Neurasthenia, Effort Syndrome) with a Description of a Simple Quantitative Method**
M. E. COHEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 496–507, Nov., 1950. 5 figs., 31 refs.

The author reports a comparison of the degree of palmar sweating, as estimated by a single recording, in three groups of subjects: 33 men with neuro-circulatory asthenia (NCA) who had been under psychiatric or medical care in military hospitals; 54 healthy men in military service who were sent to the laboratory for special study as controls; and 30 healthy hospital workers employed as controls to test for the influence of familiarity with hospital surroundings and procedures. The method of estimation was to weigh a small square of blotting paper on an analytical balance before and after it had been pressed to the palm of the hand for one minute. A number of tests were made on the rate of evaporation from the blotter, the influence of room conditions on the results of measurement, and other factors in the experiment. From these it was inferred that these factors did not materially affect results.

The mean value for palmar sweat in patients with NCA was about the same as that in the military control group. In the hospital control group, however, there was a significantly lower mean. The patients and servicemen from outside the hospital, in other words, had moist palms, while the workers who were accustomed to the hospital had not. Tests in 12 cases of thyrotoxicosis gave a mean value slightly higher than, and in a patient with hyperhidrosis a value three times as high as, the value in the NCA group.

It is concluded that the discovery of moist palms at the first clinical examination cannot be used as a reliable diagnostic feature in NCA. The results of the experiment are held to support the popular view that moist palms may be present in normal people at interview, or during examination by a physician, without signifying NCA or anxiety neurosis.

[There are several important variables in this experiment which have not been reckoned with. The hand temperature of the subjects employed was not measured, and there was no assessment of the subject's emotional state at the time of the experiment.] *Desmond O'Neill*

2110. **Psychological Treatment in Skin Disorders, with Special Reference to Abreactive Techniques**
H. J. SHORVON, A. J. ROOK, and D. S. WILKINSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1300–1304, Dec. 9, 1950. 15 refs.

Though much has been written about the place of emotional tension in the aetiology of skin disorders, there have been few accounts of the efficacy of psychotherapy

in their treatment. This paper is a report of the results of treatment by abreactive methods of 50 patients with a variety of skin disorders. The criteria for selection of cases were: the probability of a strong psychogenic element in the causation; onset sudden or apparently related to a specific traumatic incident; age under 40. The methods used were: intravenous barbiturates, ether, intravenous methamphetamine, and carbon dioxide, alone or in various combinations. Ether was found to be effective in the production of an intense, excitatory abreaction with the release of tension, anxiety, and aggression. The patient was prompted to relive painful incidents from his past life, and was deliberately encouraged to shout, cry, and struggle; during the treatment the physician kept on the alert to play upon incidents of high emotional content which might become evident for the first time in the course of the abreaction. If the treatment is a success the patient experiences a relief of tension. For the obsessional patient methamphetamine was found to be useful.

The skin disorders included urticaria, neurodermatitis, pruritus, and acne. In 21 patients the skin cleared under psychotherapy (although 3 relapsed within a year); in 22 the condition improved; and in 7 there was no change. In some cases, although the skin disease itself was unaltered, the patient was helped towards a more reasonable attitude towards it. This is especially likely to occur in certain cases of eczema in which mental tension may perpetuate an eruption initially precipitated by some occupational hazard. The authors have been impressed with the rapidity with which good results are obtained by this treatment and the infrequency of recurrences. On the whole, patients with neurodermatitis responded after a few treatments; those with pruritus required a longer time. Five illustrative case histories are given.

[The literature on the psychiatric aspect of dermatology has been in the main concerned with the psychogenesis of skin lesions; many papers are written around small groups of cases and are rather speculative. In contrast, this study is admirably realistic and practical. The analysis of the differential response to treatment of each disorder which the authors hope to make after a longer follow-up period will be most welcome.]

Desmond O'Neill

2111. **Symptom Specificity and Bodily Reactions during Psychiatric Interview**

R. B. MALMO, C. SHAGASS, and F. H. DAVIS. *Psychosomatic Medicine* [*Psychosom. Med.*] **12**, 362–376, Nov.–Dec., 1950. 8 figs., 7 refs.

This study is complementary to an earlier investigation by the same authors (*Psychosom. Med.*, 1949, **11**, 25), in which they took recordings of several physiological variables from 74 psychiatric patients in an experimental stress situation. The results of this investigation were held to support the theory of symptom specificity: that is, that the physiological mechanism underlying the patient's symptom is readily activated by stress, even though the symptom itself may not appear. In the present study 3 patients were examined at length, electromyographic tracings being taken synchronously with sound recordings during successive psychiatric interviews, with the aim of determining whether tensional responses in an area of symptom reference are more closely related to changes in the degree of stress than tensional responses in other body areas.

The first patient had headache as a presenting symptom. During the early interviews forearm and forehead tension rose together; after this, forearm tension fell steadily, while forehead tension rose sharply during two later interviews especially designed to provoke anxiety. High-level and sustained contraction of the frontalis was observed to be associated with headache. In one of these two interviews forehead tension began to rise at the outset, though the patient did not complain of headache until it reached a peak; during this same period tension in the forearm fell. Talking was as a rule accompanied by a fall in forehead tension, and pauses with a rise to the former level. In the two other case records given, some further instances of the relation between muscle tension and the patient's behaviour at interview are noted. In the third patient an experimental stress (pain) did not cause an increase in tension in the symptom area, whereas discussion of his own life experiences usually did; for this patient, therefore, the precipitant of symptoms was a specific stress and not merely any unpleasant happening. The temporal relations of changes in tension in the first and second patients are compared; in the first case tension changes were slow, but in the second (a hysterical subject) tension rose rapidly when the patient wanted to end the interview and fell as abruptly later. This is considered to illustrate the difference, in physiological terms, between a chronic anxiety state and a conversion hysteria.

Desmond O'Neill

2112. **Biochemical Individuality. V. Explorations with Respect to the Metabolic Patterns of Compulsive Drinkers**

E. BEERSTECHER, H. E. SUTTON, H. K. BERRY, W. D. BROWN, J. REED, G. B. RICH, L. J. BERRY, and R. J. WILLIAMS. *Archives of Biochemistry* [*Arch. Biochem.*] **29**, 27–40, Nov., 1950. 31 refs.

A preliminary study was undertaken at the University of Texas to determine whether there was any basis for the suggestion that alcoholism results from the possession of a distinctive, inheritable metabolic pattern which predisposes towards the disease. To make the study feasible the investigation was limited to 8 controls and 4 compulsive drinkers; all were males between 16 and 39 years old and, apart from the alcoholic traits of the latter group, were healthy individuals. Approximately 60 different estimations related to metabolism were made on each of the 12 subjects 5 days a week over a period of 4 weeks; these items involved biochemical studies of urine, saliva, and blood, and included determinations of the taste thresholds for hydrochloric acid, sodium chloride, potassium chloride, creatinine, and sucrose. The concentrations of sodium, potassium, calcium, magnesium, iron, copper, aluminium, and phosphorus in the blood serum were determined, while the urine estimations included 24-hour volume, specific gravity, *p*H, and creatinine, alanine, citrulline, glutamic acid, glycine, serine, taurine, sodium, chloride, sulphate, phosphate, citrate, lactate, hippurate, urate, urea,

glucose, aneurin, pantothenic acid, and gonadotrophin content; assays of 16 different substances in the saliva were also performed. In each case a mean value was calculated for each subject and for the two groups. No attempt was made to control the diet of the subjects, partly for practical reasons, but also because it was desired not to eliminate self-selection of food as a physiologically significant phenomenon. The intention was to investigate many items in a few individuals by rapid methods capable of revealing gross differences, and a number of analytical methods involving paper chromatography were developed for this purpose.

The results obtained were treated statistically, and 11 items were found for which the probability of the observed differences between alcoholics and non-alcoholics being due to chance was only 1 to 10%, and 9 for which the corresponding probability was 10 to 20%. In 6 cases the difference was statistically significant (probability 5% or less), whereas no more than 3 such differences (5% of 60) would be expected to occur by chance. Hence the findings suggest strongly that compulsive drinkers do have distinctive metabolic characteristics. The saliva sodium and uric acid content, the urinary *p*H and urate, hippurate, citrate, aneurin, and pigment content, together with the blood serum magnesium level appear to be elevated in alcoholism, whereas blood phosphorus and urinary gonadotrophin, taurine, and citrulline levels seem to be decreased. Increased taste sensitivity to sodium chloride also appears to be associated with alcoholism. *R. P. Hullin*

2113. **Evaluation of Electric Convulsion Therapy as Compared with Conservative Methods of Treatment in Depressive States**

S. KARAGULLA. *The Journal of Mental Science* [*J. ment. Sci.*] **96**, 1060–1091, Oct., 1950. 8 figs.

Out of a total of over 4,000 cases treated at the Royal Edinburgh Hospital for Mental and Nervous Disorders between 1932 and 1948 the author studied the records of 923 in which the diagnosis of depressive state seemed justified, all cases having shown a manic phase at any time being excluded and records giving data insufficient for reliable diagnosis being discarded. The cases were analysed according to sex, age, history, type of treatment (conservative or convulsive), number of admissions (followed back to 1900 for females and 1911 for males), duration of illness, mental state after treatment (recovered, improved, not improved, or died). The patients were, if possible, followed up to November, 1949, the after-history being obtained in 80% of cases. Two control groups, the first of depressives admitted before the introduction of electric convulsion therapy (E.C.T.) in 1940, and the second of those admitted after that date but who were unfit for E.C.T., were studied.

Of the 923 patients, 61% were admitted to hospital once only; out of 1,611 admissions, in 80 to 90% of cases the patient was discharged recovered or improved; large numbers stayed no more than 6 weeks in hospital. With regard to treatment, the percentage of cases remaining in hospital was almost identical in the control groups and the group receiving E.C.T., the rates of recovery showing no statistically significant difference. The use of E.C.T. did not shorten the duration of hospitalization significantly, and up to 12 months after discharge there was a higher incidence of relapse among those regarded as "recovered" in the E.C.T. group than in the control groups. The percentage of relapses after the first year in all groups was dependent upon the number of previous admissions and on the length of time during which the patient was followed up. The author points out that in many cases discharged "recovered" after E.C.T. the long period intervening between cessation of treatment and discharge cast some doubt on the role of convulsive therapy as a contributory factor. Suicide occurred most frequently during treatment in the control group and after discharge in the E.C.T. group, but the author states that the figures for suicide after discharge may not be accurate as some cases may have occurred among the patients untraced.

The author concludes that E.C.T. frequently ameliorates symptoms and renders the illness more bearable, but that it should apparently not be given until 6 to 8 weeks after admission, and that a second course should not be given until a further 3 months has elapsed.

[This important and detailed research is probably the most accurate investigation so far published with regard to the treatment of depression with E.C.T. The original should be consulted and compared with the reports of Hinko and Lipschutz on the shock treatment of manic-depressive cases, and of Fishbein on that of involutional depressives.] *G. de M. Rudolf*

2114. **Frontal Block. Some Observations on the Effects of Local Anaesthetic Injections into the Cerebral Hemispheres of Rabbits and Psychotic Patients**

J. S. B. LINDSAY. *The Journal of Mental Science* [*J. ment. Sci.*] **96**, 923–934, Oct., 1950. 1 ref.

In the first section of this paper some animal experiments are described. These were carried out in 1947 without knowledge of the work of Soulairac and Barbizet on rats (1946). Subsequently eight infiltrations of the white matter of the frontal lobes have been carried out with local anaesthetic agents (in 3 psychotic patients). On some occasions there was immediate improvement, and in others improvement only after a period of altered conduct. The duration of the benefit over several days is noteworthy. The first case showed immediate benefit, but the repeated infiltration led to confusion. The second case showed some benefit, which was sustained for weeks, apart from one of his short excited episodes. In the third case four injections were more effective in controlling behaviour over a 6-week period than 12 electric convulsion treatments (E.C.T.) in the preceding 6 weeks, and an equal number of E.C.T. in the subsequent 6-week period.—[Author's summary.]

2115. **Postnatal Cerebral Trauma as an Etiological Factor in Mental Deficiency**

W. H. BOLDT. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **55**, 345–365, Jan., 1951. Bibliography.

Infectious Diseases

VIRUS INFECTIONS

2116. **Experimental Epidemiology of Influenza in Mice. II. The Increase of Virus in Nasal Mucus Membrane.** [In English]
K. NAKANISHI. *Kitasato Archives of Experimental Medicine* [*Kitasato Arch. exp. Med.*] **23**, 127–129, Oct., 1950.

When mice are inoculated intranasally with W–S strain of influenza-A virus very little virus is detectable in the nasal mucosa shortly after instillation. By the third day after inoculation the amount of virus in the nasal mucosa has increased considerably, whereas the virus titre in the lungs is still low. It is concluded that influenza-A virus actually multiplies in the nasal mucosa.
G. M. Findlay

2117. **Aureomycin Treatment of Complications following Vaccination against Smallpox.** (Aureomycinbehandling av komplikationer efter smittkoppsvaccinering)
B. L-K APPELBOM and M. SCHNABEL. *Nordisk Medicin* [*Nord. Med.*] **44**, 1790–1792, Nov. 10, 1950. 17 refs.

Aureomycin in daily doses of 50 mg. per kg. body weight was given for 2 to 4 days to 4 young children suffering from complications after vaccination. The complications were secondary lesions around the vaccination site in one case, and on the head, face, hands, and legs in the others; fever, adenitis, and conjunctivitis were also observed. There was a radical improvement in all cases.
W. G. Harding

2118. **Postvaccinal Encephalitis in Infancy**
H. J. LAWLER. *Journal of Pediatrics* [*J. Pediat.*] **37**, 709–710, Nov., 1950. 7 refs.

2119. **Gamma Globulin in the Prevention and Attenuation of Measles. Controlled Trials in Day and Residential Nurseries**
MEDICAL RESEARCH COUNCIL. *Lancet* [*Lancet*] **2**, 732–736, Dec. 9, 1950. 7 refs.

A report to the Medical Research Council records the result of a trial of gamma globulin, prepared at the Lister Institute by the ether-extraction method of Kekwick and Mackay, for the purpose of modifying measles in child contacts in day nurseries. In a series of carefully controlled trials gamma globulin was injected in doses of from 225 to 450 mg. into 212 susceptible measles contacts between the ages of 6 months and 5 years. Of these, 31·6% developed measles, 94% of them showing modification described as excellent or satisfactory. It is shown that the attack rate in protected children is a function of the dosage. In those receiving 225 mg. it was 33·7%, in those receiving 450 mg. 21·6%, whereas in corresponding groups who received 5 ml. of adult serum the attack rates were 55·4% and 65·8%. Moreover, it is shown that the duration of passive immunity also depends on dosage; with large doses some degree of protection is obtained up to 6 weeks.

It was noted that dried globulin retains its potency unimpaired for at least 9 months.

On the basis of these trials the authors recommend the following scale of doses in mg.:

Age (Months)	Modification	Prevention Probable	Prevention Sure
6 to 23	150 to 225	450	675
24 to 59	225 to 300	675	900

Reactions were inconspicuous and no serious complications occurred in protected groups. As gamma globulin is so expensive its use must be restricted to limiting outbreaks in local child populations under 5 years of age.
Joseph Ellison

2120. **The Lung in Measles.** (Le poumon dans la rougeole)
P. SÉDALLIAN, P. MARAL, —. DE L'HERMUZIÈRE, and —. TRAEGER. *Pédiatrie* [*Pédiatrie*] **39**, 112–116, 1950. 6 refs.

The authors have studied radiographs of the lungs in 71 cases of measles. The age distribution was as follows: under 5 years, 46 cases; 5 to 10 years, 12; 10 to 15 years, 4; and over 15 years, 9 cases. The investigations usually commenced in the fully eruptive stage, but occasionally later. Radiographs were taken on the 1st, 2nd, 3rd, 4th, and 5th days after the onset of the rash, and in most cases up to the 15th to 20th days. To eliminate confusion with tuberculous shadows, patch tests were taken at the end of the illness, which was assumed to be on the 15th day, and these were negative in all but 3 cases.

The following radiological observations were made: (1) in 37 cases there was an increase of the hilar shadow with accentuation of the pulmonary striation; (2) in 11 cases there were parenchymatous shadows of the type associated with pulmonary congestion and lobar or bronchopneumonia; (3) in 2 cases there were granular shadows; (4) in 2 cases the picture resembled bullous emphysema; (5) in 5 cases there were pleural shadows with accentuation of the fissures; (6) in 1 case the appearance was of atelectasis; (7) in 13 cases there was no apparent abnormality.

The authors discuss the persistence and development of these radiological findings and compare their results and conclusions with the original work done by Kohn and Koiransky (*Amer. J. Dis. Child.*, 1929, **38**, 258; 1931, **41**, 500; and 1933, **44**, 40.

The parenchymatous shadows disappeared in a few days, but all the other types regressed slowly over a period of several months. Children of 5 years and under showed the abnormalities more often and with greater intensity than the older age groups. *E. R. Cole*

2121. **Hepatic Lesions in a Child Born of a Mother Suffering from Infective Hepatitis during Pregnancy.** (Epatopatia in nato da madre affetta da epatite epidemica in gravidanza)
F. TOSCANO and G. ROSSI. *Pediatria* [*Pediatria*] **58**, 209–219, March–April, 1950. 5 figs., 17 refs.

A woman of 34 in the 7th month of pregnancy complained of loss of appetite, nausea, and acute abdominal pain, rapidly followed by a subicteric colouring of the sclerae, urobilinuria, and slight hepatomegaly, but no splenomegaly. She was treated with nicotinamide, ascorbic acid, vitamin K, glucose and insulin, "urotropine", and sulphaguanidine. The signs and symptoms increased, the urine became darkly stained with bile pigments, and the liver continued to enlarge. After 2 or 3 weeks her condition rapidly became worse, with frequent attacks of cardiovascular collapse. The serum bilirubin content, which was initially 0·7 mg. per 100 ml., increased to 2·2 mg. per 100 ml. Albumin and casts appeared in the urine. The Wassermann reaction was negative. Some days later the general condition improved, with a reduction in jaundice and in the size of the liver. She gave birth to a child a few days later, after about 8 months' pregnancy, at which time there was still jaundice and slight urobilinuria. The infant weighed 1·4 kg. and was heavily jaundiced. The urine contained a small amount of bile pigment, and the liver was enlarged to 3 fingers. On the second day the bilirubinaemia was 1·2 mg. per 100 ml., rising to 2·05 mg. per 100 ml. on the next day. There was no pyrexia and blood culture was negative. The child died on the 6th day.

After careful and comprehensive microscopical examination of the liver, the authors concluded that the infection had not been transmitted from the mother through the placenta, but that the hepatic condition in the infant was due to a "general toxic action" resulting from the condition of the mother. *E. R. Cole*

2122. **Measurements of Respiratory Paralysis in the Poliomyelitis Epidemic of 1948.** (Untersuchungen über die Atemlähmung bei der Poliomyelitisepidemie 1948)
W. BOLT and H. VALENTIN. *Klinische Wochenschrift* [*Klin. Wschr.*] **28**, 113–118, Feb. 15, 1950. 4 figs., 36 refs.

Respiratory paralysis in poliomyelitis cases was subjected to exact spirographic analysis. The oxygen uptake, respiratory frequency, respiratory volume, respiratory minute volume, respiratory limiting value (maximum possible ventilation per minute), and vital capacity were measured for respiration of ordinary air and of oxygen. If the oxygen uptake per unit of time is higher with oxygen than with air-breathing, respiratory insufficiency is present and artificial respiration is therefore indicated. The efficacy of the various artificial-respiration instruments was examined. Biomotor respiration was found inadequate in severe respiratory disturbances and inferior to the "iron lung". Even in the latter, however, it is not possible to abolish respiratory insufficiency entirely; in such cases oxygen must be given as well. To diminish the dead space, the administration of oxygen through a tracheotomy cannula is sometimes indicated. Detailed analysis of respiratory function permits greater precision in the indications for use of the respirator. —. *Zellweger* (*Excerpta Medica*)

2123. **The Incidence of a Normal Spinal Fluid in Acute Poliomyelitis**
E. E. NICHOLLS. *Journal of Pediatrics* [*J. Pediat.*] **37**, 894–898, Dec., 1950. 4 refs.

Owing to the increased incidence of poliomyelitis there has arisen some confusion as to the positive criteria for its diagnosis, particularly in respect of changes in the cerebrospinal fluid (C.S.F.). Out of 320 cases seen during the period 1944 to 1949 the C.S.F. was normal in 64. In 8 of these cases the acute stage had passed, but in 22 of the remaining 56 the C.S.F. was examined again the next day, and was found to be abnormal (in cell and/or protein content) in 13. There remained 43 patients (13·8%) with negative C.S.F. findings in the face of a positive clinical diagnosis, 4 of them being known contacts. In order to obtain the fullest information from examination of the C.S.F. the author stresses: (*a*) that the fluid should be examined immediately after withdrawal; (*b*) that the clinical stage of the disease at the time of examination must be known, because the fluid may be normal during the first 24 hours but abnormal if tested again the next day; and (*c*) that bizarre results may, however, be obtained at re-examination. [This is a common enough finding in many conditions unrelated to poliomyelitis.]
D. P. Jones

2124. **Studies on Entry and Egress of Poliomyelitis Infection. III. Excretion of the Virus during the Pre-symptomatic Period in Parenterally Inoculated Monkeys**
H. K. FABER, R. J. SILVERBERG, L. A. LUZ, and L. DONG. *Journal of Experimental Medicine* [*J. exp. Med.*] **80**, 571–589, Dec., 1950. 4 figs., bibliography.

The excretion of poliomyelitis virus in the stools and nasopharangeal secretions of patients with either acute or "atypical" poliomyelitis has been well established for some time. Virus is present also in the cells lining the intestine and nasopharynx, but the pathways by which virus reach the gut are not definitely known. In the present paper the authors describe experiments designed to show whether virus is released into the gut after multiplication in extraneural tissues or whether it is secreted directly from nerve cells.

Excretion of virus in stools and nasopharyngeal washings was studied in groups of cynomolgus or rhesus monkeys after parenteral inoculation of virus. The strains used, Cam and Wis '45, had previously been shown to be infective by mouth, although in the present experiments all inoculation methods were designed to avoid primary infection from the alimentary canal.

When virus was given by infraorbital nerve dip, excretion could be demonstrated in both faeces and nasal washings within 2 to 4 days of exposure; after inoculation into the Gasserian ganglion 1 of 4 monkeys excreted virus in stools and washings after 4 days; on inoculation into the coeliac ganglion, virus was found in the stools of 2 monkeys after 4 and 7 days and persisted for 3 days; on intrathalamic inoculation, excretion was demonstrated at 4 to 5 days in 2 of 3 experiments, and in both cases excretion preceded the appearance of symptoms. After intravenous inoculation of large doses of virus, however, no excretion was demonstrable and it therefore seems unlikely that virus reaches the alimentary tract through the blood stream.

It is concluded from these experiments that multiplication of virus takes place in peripheral ganglia which supply the nerve fibres of the alimentary canal. The concept of peripheral ganglia serving as both site of entry and immediate source of excretion of virus into the alimentary tract may explain several previously puzzling clinical observations. It is thus possible for multiplication to occur in the ganglia without involvement of the central nervous system, and hence virus may be excreted without obvious clinical signs. The virus present in the stools is most probably derived from swallowed pharyngeal secretions, but there is some evidence of direct excretion into the gut. The mode of elimination is by centrifugal spread through the axons of peripheral nerve fibres, and not through either the blood or lymphatic system. Excretion can therefore be explained on the basis of axonal conduction without resort to the hypothesis of extraneural multiplication.

J. F. McCrea

2125. **Poliomyelitis following Inoculations**
F. M. BURNET. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 775–782, Nov., 1950. 1 fig.

See also Section Hygiene and Public Health, Abstract 1771.

2126. **Serological Response of Human Beings and its Persistence to Japanese B Encephalitis Ether Extracted Chick Embryo Vaccine.** [In English]
H. HAYASHI and H. OZAWA. *Kitasato Archives of Experimental Medicine* [*Kitasato Arch. exp. Med.*] **23**, 115–122, Oct., 1950.

Vaccines treated with formalin and prepared from mouse-brain or chick-embryo tissues containing Japanese type-B virus are known to produce a good antibody response. In a series of experiments carried out at the Kitasato Institute for Infectious Diseases, Tokyo, a chick-embryo vaccine consisting of a 20% emulsion in phosphate buffer at *p*H 7·0 was extracted with one and a half volumes of ether. The water-soluble phase of the mixture was separated off and the residual ether removed under negative pressure. About one-half of the persons receiving this vaccine, which is below the minimal potency requirements of the Japanese National Institute of Health, show antibody response. The most effective method is to give 2 doses of 0·1 ml. intracutaneously. In an epidemic area there is a natural rise in immune bodies from early May to the end of the epidemic season owing to the occurrence of latent infections. If a true measure of the potency of any vaccine is to be obtained, vaccination should not be carried out during the epidemic season.

G. M. Findlay

BACTERIAL INFECTIONS

2127. **Meningitis due to *Pseudomonas aeruginosa* Treated with Polymyxin B**
E. R. HAYES and E. YOW. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 633–637, Dec., 1950. 1 fig., 11 refs.

Streptomycin has not proved entirely satisfactory in the treatment of infections due to *Pseudomonas aeruginosa*. If this fails polymyxin B should be administered. Polymyxin B was given to a patient with meningitis due to *Ps. aeruginosa* following appendicitis and bacteriaemia, after penicillin, aureomycin, streptomycin, and sulphadiazine had all failed. The dosage was 80 mg. intramuscularly every 6 hours and 2 mg. intrathecally every 12 hours. After 24 hours the intramuscular dose was reduced to 40 mg. every 4 hours and continued for 9 days. The total dose intramuscularly was 2·2 g. The cerebrospinal fluid became sterile after 24 hours of polymyxin therapy. Nausea was controlled by pyribenzamine, but albuminuria occurred.

G. M. Findlay

2128. **Extrarenal Azotemia in Cholera**
H. SENECA and E. HENDERSON. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 855–861, Nov., 1950. 12 refs.

Cholera may cause either extra-renal azotaemia, in which there is no other evidence of renal damage, or extra-renal uraemia, in which the picture of renal failure develops. After a brief review of the pathology of lower nephron nephrosis, the authors describe 6 patients with cholera who developed extra-renal azotaemia without typical uraemia, all of whom recovered. The impairment of renal function may be due to dehydration and ischaemia or to the action of the endotoxin, especially on the kidney. Dehydration can act both by causing functional renal insufficiency and by increasing protein catabolism, and can therefore provide a satisfactory explanation of the extra-renal azotaemia of cholera. *J. L. Markson*

2129. **Experiments with Antibiotic-killed Cholera Vaccines**
O. FELSENFELD, V. M. YOUNG, and S. J. ISHIHARA. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 863–864, Nov., 1950. 2 refs.

Experiments were carried out on two cholera strains isolated during the 1947 Egyptian cholera epidemic. Both were killed by 7·28 units of streptomycin, 6·25 units of aureomycin, or 3.12 units of neomycin per ml. of trypticase broth in which the organism was grown. Vaccines were prepared by adding three such minimal

killing doses of the antibiotics to each ml. of *Vibrio cholerae* (*V. conna*) suspension containing 8,000 million organisms per ml. These vaccines, tested in mice, compared favourably with the standard vaccines. Since neomycin is the antibiotic of choice, a large scale mouse experiment was carried out using the neomycin-killed vaccine. This proved to be at least as effective as the standard formolized and phenolized vaccines.

J. L. Markson

2130. **The Gastrointestinal Syndrome of Chronic Brucellosis**

H. GAUSS. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **17**, 323–332, Oct., 1950. 6 figs., 18 refs.

In this paper from Denver it is stated that brucellosis is endemic in Colorado. Using an intradermal injection of "brucellergen" as his chief diagnostic test, the author finds that many patients with gastric or biliary dyspepsias, with the irritable colon syndrome, and with mixed patterns of intestinal dysfunction are suffering from brucellosis. Twenty such cases are described in which blood culture was negative and serum antibody levels normal. Treatment with brucellin, a soluble *Brucella* culture filtrate, and aureomycin are advocated, but results are often disappointing.

[Throughout this paper it is assumed that because a patient has gastro-intestinal symptoms and because he has a positive skin reaction to a *Brucella* antigen, his symptoms must be due to brucellosis. No pathological or therapeutic evidence is produced to show that this assumption is correct. Therefore, in view of the frequency of functional gastro-intestinal disorders everywhere and the apparent endemicity of brucellosis in Colorado, the author's conclusions must be accepted with reserve.] *J. Naish*

2131. **The Treatment of Scarlet Fever with Penicillin G Administered Orally Three Times a Day**

L. WEINSTEIN and T. S. PERRIN. *Journal of Pediatrics* [*J. Pediat.*] **37**, 844–853, Dec., 1950. 32 refs.

Penicillin was administered in a variety of dosage schedules to 356 patients suffering from scarlet fever, of whom 9 were severely, 294 moderately, and 53 mildly ill. Seven different scales of oral dosage were used ranging from 50,000 units to 800,000 units every 8 hours, and one group were given 100,000 units intramuscularly every 8 hours. [Details are not supplied of the numbers in each of the treatment groups, the method of allocation, or the distribution in regard to severity.] The patients recovered rapidly from their illness as judged by the subsidence of fever, the disappearance of throat symptoms, and the return of the leucocyte count and erythrocyte sedimentation rate to normal. Of 246 patients (69%) whose throat swab showed type β haemolytic streptococci on admission, 229 became negative after 24 hours therapy. Complications included 5 cases of catarrhal otitis media, 3 of recurrent tonsillo-pharyngitis, and 1 of recurrence of scarlet fever.

The authors conclude that these beneficial effects were the result of the treatment administered. [No credit appears to be given to the mild character of scarlet fever in present practice. In the whole of the United States the annual number of deaths is now about 100, which suggests that there, as in Britain, the prevalent form is exceedingly mild.] *T. Anderson*

2132. **The Treatment of Diphtheria Carriers with Tyrothricin.** (La tirotricina nella sterilizzazione dei portatori difterici)

L. BAGLIONE and F. DI NOLA. *Minerva Medica* [*Minerva med., Torino*] **41**. 1071–1074, Nov. 24, 1950. 12 refs.

The problem of the diphtheria carrier is an old one, and the methods of treatment numerous; local applications, antitoxic and antibacterial sera, ultraviolet light, and tonsillectomy have their advocates. Until recently the method used at the Infectious Diseases Hospital at Turin has been a combination of methylene blue and ultraviolet light, the dye both acting as an antiseptic and facilitating the penetration of the rays. Lately penicillin by various routes has been tried with good results, but its action is slow. On the other hand, a semicarbazone compound, active *in vitro*, was disappointing. [Unfortunately, sensitivity *in vitro* is no guide to a similar action *in vivo* where the upper respiratory tract affords ample protection to the offending organism.]

Tyrothricin is the latest effective agent. In the present investigation 3 ml. of a 1 in 2,000 solution was given twice daily as an aerosol spray. Throat swabs were taken at the end of 4 days and again as necessary until three negatives had been obtained. Of 100 patients only 2 remained refractory, and as many as 54 were rendered negative after only 4 days' treatment. In general, convalescent patients harboured the less virulent organisms, which were easier to remove, while the slower and refractory results occurred in the healthy carrier with highly virulent bacilli. The method is difficult to carry out in younger patients, but appears to be free from toxic effects. *A. Paton*

See also Section Pharmacology and Therapeutics, Abstract 1822.

2133. **Gangrene of the Extremities. A Recently Recognized Complication of Severe Meningococcic Infection**

H. A. WEINER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 877–890, Dec., 1950. 3 figs., 42 refs.

Gangrene of the skin is a well-known complication of meningococcal septicaemia, but gangrene of the extremities is rare, only 9 cases having been reported since 1944. A 28-year-old negro was admitted to hospital in semi-coma, with a blood pressure of 50/40 mm. Hg. Lumbar puncture revealed a severe meningitis and he was treated with sulphadiazine intravenously and aqueous penicillin intramuscularly. In a few days the patient's condition improved, but as he recovered consciousness he complained of pain and tenderness in his feet, and 4 days after admission gangrene of the toes of the left foot developed. Peripheral vascular studies showed no impairment of the circulation in the foot, and lumbar sympathetic block on two occasions gave negative results. The local

condition gradually deteriorated and 8 days later pulsation was absent in the dorsalis pedis artery. Amputation was subsequently carried out. The Wassermann reaction was negative; the first blood culture was positive and subsequent ones negative.

It appears from the literature that this type of gangrene in meningococcal infection has an equal sex incidence, and that most of the cases are in young adults. The presence of meningitis is not essential, but the patient in every case reported has been seriously ill before the onset of gangrene and in this case would certainly have died but for chemotherapy. The toes are always involved; the fingers to a less degree. There is little doubt that the condition is related to the severity of the septicaemia and is due to embolism. *Paul B. Woolley*

TUBERCULOSIS

2134. **Tuberculosis in Jersey**
R. N. McKinstry. *Tubercle* [*Tubercle, Lond.*] **31**, 272–278, Dec., 1950. 3 figs., 8 refs.

Jersey has a population of approximately 57,000, mainly of Breton and Norman stock; the proportion of Bretons is increasing. Since 1910 the mortality from tuberculosis in this population has been consistently higher than in England and Wales, but lower than in France until recent years, when there was a considerable reduction in the rate in France. In 1924 the mortality in Jersey from all forms of tuberculosis was 134 per 100,000; in the next 15 years the rate fell to 60, but rose again during the war years to between 120 and 140. Since the end of the war it has again been falling, and in 1948 was 68.

The author discusses some of the factors which might account for the higher rate in Jersey than in England and Wales. There is little evidence that poverty is more serious and widespread in Jersey than in England. Nutrition appears to be no worse in Jersey—on the contrary, comparison of the height and weight records of elementary school-children shows Jersey children to be taller and heavier than English children of corresponding age. Overcrowding, acknowledged to be an important factor in tuberculosis, is on the evidence less severe than in England. The author quotes evidence of high susceptibility to tuberculosis in Celtic populations, including Bretons, and he believes that the high proportion of Bretons in the Jersey population may be in part responsible for the high tuberculosis rate. Jersey herds are virtually free from tuberculosis, and the author suggests that the low rate of immunization by bovine tuberculosis in childhood may be responsible for the relatively high rate in adults. [He ignores the fact that in the U.S.A., where bovine tuberculosis has been almost eradicated, the tuberculosis rate is well below that for England and Wales.]

The results are given of a tuberculin survey in 2,508 children and adults. In the age group 0 to 5 years, 2·9% gave positive reactions to 10 units of tuberculin; at 5 to 10 years, 12·7% were positive; at 10 to 15, 23·6%; at 15 to 20, 32·6%; and at 20 to 30, 78·7%. B.C.G. vaccination has been offered to all non-reactors who desire it. The vaccine is given intradermally. No attempt is made to segregate the vaccinated unless there is definite evidence of open tuberculosis in their immediate environment. *M. Daniels*

2135. **Report on 1,137 Cases of Pulmonary Tuberculosis Treated by Thoracoplasty at Bruges since 1926.** (Rapport sur 1,137 cas de tuberculose pulmonaire traités par thoracoplastie, à Bruges, depuis 1926)
L. de Winter. *Acta Tuberculosea Belgica* [*Acta tuberc. belg.*] **41**, 165–214, Nov., 1950. 29 figs.

An analysis is presented of 1,137 cases of pulmonary tuberculosis treated by thoracoplasty since 1926 at the Hôpital Saint-Jean, Bruges. From 1926 to 1932 the technique of thoracoplasty used was the then generally accepted one of Sauerbruch. In 1932 this was replaced by the more radical method developed by Sebrechts, in which a considerable part of several upper ribs is removed, often as far back as the costovertebral joint, with the object of obliterating the paravertebral gutter. This was carried out in several stages and in some cases was preceded by an apicolysis reinforced with pectoral muscle. This technique generally ensured the obliteration of large apical cavities. Deaths occurring within 3 months of the last stage of operation are classed as post-operative deaths and numbered 249 (22%), of which deaths in cases classed as "good" and "fair" operative risks each constituted 3%. The rate fell from 28·2% for the first 5 years of the 22-year period to 13·2% for the last 5 years. The main cause of these deaths was right-sided heart failure attributed to loss of elasticity of the walls of pulmonary blood-vessels in the collapsed area. The main cause of death occurring later than 3 months after operation was an exacerbation of pulmonary tuberculosis. The over-all survival rate one year after operation was 88% among the patients regarded as good operative risks, 70% among those regarded as bad risks; after 3 years these rates were 77% and 32% respectively; after 10 years 61% and 18%; after 15 years 45% and 14%; and after 20 years 39% and 11%.

The author stresses the achievement of a 3-year survival-rate of 32% among cases which in other hands would probably not have been considered fit for surgical treatment. He claims that such results could not have been achieved by collapse measures any less radical.
J. M. Alexander

2136. **A Controlled Investigation of Streptomycin Treatment in Pulmonary Tuberculosis**
E. R. Long and S. H. Ferebee. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 1421–1451, Nov. 3, 1950. 5 figs.

In July, 1947, the Tuberculosis Study Section of the U.S. National Institutes of Health was asked to plan and direct clinical trials of streptomycin therapy in the treatment of tuberculosis. By March, 1950, observations over a period of 12 months had been completed in a total of 541 patients, and the authors here present a preliminary analysis of the results. Physicians in different parts of the country who participated in the

trial adopted a common scheme of treatment and made uniform observations at uniform intervals. The inquiry included " the broad range of pulmonary tuberculosis, excluding only minimal disease at one extreme and terminal disease at the other ". The clinical investigators submitted *x*-ray films and other findings in cases which they considered suitable for the study, the choice being made by a central panel. It was determined by chance for each hospital whether a case should be allocated to the streptomycin or control group. Patients in the former group were given 20 mg. of streptomycin per kg. body weight for 91 days. In addition, all patients in both groups received any other form of therapy, including collapse therapy and surgical procedures, which the individual clinician thought was indicated.

About 40% of the patients were negroes, and there were slightly more males than females. Approximately half of the patients were between 25 and 44 years of age. Surgical or collapse procedures had been used in about one-fourth of the cases in each group at the time of selection for study. Nearly half of both groups were judged to have predominantly caseous disease; the disease in most of the others was predominantly exudative, being fibrotic only in a small remainder. The disease was classified as acute in two-fifths of the total, subacute in another two-fifths, and chronic in the rest. The number of patients in the control group leaving hospital against medical advice during the period of the trial was 35, compared with 22 in the streptomycin group.

During the 12-month observation period 21 deaths occurred in the streptomycin group and 40 in the controls, but the difference in mortality was confined almost entirely to the first 6 months of observation, when 26 controls and only 8 treated patients died. The mortality was higher among males than females, and higher among non-whites than among whites. The control group showed a much slower decrease than the streptomycin group in the proportion of markedly febrile patients, but at the end of 12 months contained fewer patients with temperatures above 99·6° F. (37·6° C.) than the streptomycin group (the greater number of deaths must, however, be taken into account). Loss of fever was much less common among the controls than among the streptomycin group. At the end of 12 months 24·5% of the controls were bacteriologically negative, as against 38·2% of the streptomycin group. *X*-ray changes were evaluated by a panel of four radiologists. There was lack of agreement in a large number of cases, in which the percentage distribution of opinion was taken as the index of radiological status. In the streptomycin group about seven-tenths had improved by the end of 3 months; within this group there was continued improvement during subsequent periods. The proportion showing no change since the beginning of the study decreased from 16% at 3 months to about 7% at the end of 12 months; the proportion showing deterioration increased very slowly as that showing no change decreased. Among the controls, change was much slower and less dramatic. At the end of 3 months the condition of 25% of the patients was still unchanged, this proportion gradually declining to about 10% at the end of one year.

M. Daniels

2137. **Three-year Follow-up Study on 202 Cases of Pulmonary Tuberculosis Treated with Streptomycin**
R. O. Canada, S. T. Allison, N. D. D'Esopo, E. Dunner, R. E. Moyer, A. Shamaskin, C. W. Tempel, and W. V. Charter. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 563–571, Dec., 1950. 2 figs., 7 refs.

This paper records a follow-up, after 3 years, of 202 out of 223 patients treated under the U.S. Veterans Administration project. The majority of patients were young men with an acute tuberculous lesion. They received a total daily dosage of 1·8 to 2·0 g. of streptomycin for 120 days. Relapse occurred in 24% of the patients towards the end of the treatment and during the first 4 months afterwards.

After 3 years 56 patients had died of tuberculosis; in 56 the disease remained active or quiescent; in 11 it was apparently arrested; and in 64 it was arrested. The mortality in patients under 25 years of age was 35%, compared with 23% in the group over 25 years of age. However, the disease had become inactive more often in the younger group of patients who were still living 3 years after treatment (68% compared with 53% in the older group). *X*-ray examination of 101 patients showed a decrease in the degree of improvement and an increase in the degree of deterioration during the post-treatment period. Inclusion of the 4-month treatment period made a considerable difference to the degree of improvement observed. Marked improvement was noted almost three times as often during the interval from the beginning of treatment until the time of follow-up as during the interval from the end of treatment to the time of follow-up. Sputum conversion occurred during treatment in 46 of 187 patients (25%), and during the years following treatment an additional 25% became negative. There was no indication of any decrease in the incidence or degree of resistance to streptomycin during the 3 years following treatment. Of 100 patients who had vertigo or ataxia during treatment, 91 still had symptoms in some degree; in none had they become worse.

Kenneth Marsh

2138. **Dihydrostreptomycin in Pulmonary Tuberculosis**
N. S. Lincoln, R. Horton, A. M. Stokes, J. Monroe, and H. M. Riggins. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 572–581, Dec., 1950. 1 fig.

The authors gave dihydrostreptomycin (DHSM), 40 mg. per kg. body weight, in divided doses twice daily for 56 to 90 days, to 64 patients between the ages of 15 and 60 years suffering from acute, predominantly exudative tuberculosis which was moderately or far advanced. In 63 patients tubercle bacilli were found on culture of the sputum; 12 patients had lesions of the mucous membranes. The patients were examined at the end of treatment, and again 3 and 5 months after the completion of treatment. Collapse therapy and resection were carried out when considered necessary. The only toxic effects were pain, induration, and necrosis at the site of injection: these were attributed to impurities in the DHSM hydrochloride. Patients preferred injections of DHSM sulphate. No vestibular disturbances were noted. In 32 patients sputum was still positive on

direct examination or on culture. No conclusions could be drawn about the emergence of drug-resistant strains. The authors conclude that: (1) the earlier the drug was used in the pathogenetic phase of the disease the greater was the chance of favourable effect; (2) such a favourable effect, when it occurred, was seen usually between the 4th and 6th weeks; (3) there was no response or only a slight one in patients with chronic disease.

Kenneth Marsh

2139. **The Nature of the Action of Streptomycin on Tubercle Bacilli**

L. P. GARROD. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 582–585, Dec., 1950. 1 fig., 7 refs.

Streptomycin was added to Dubos's liquid medium in various concentrations, and tubes containing 5 ml. were inoculated with 0·2 ml. of a culture, in the same medium, of *Mycobacterium tuberculosis* H37 Rv. The tubes were kept in a water bath at 37° C. and viable counts were made forthwith and at intervals thereafter, using the dropping-pipette dilution method and the surface inoculation of Dubos's agar medium with a 0·02-ml. drop of each dilution. The fall in the viable count produced by 100 μg. per ml. was steep, and sterility was achieved in 8 hours. A concentration of 20 μg. per ml. killed more slowly, sterility being demonstrated at 24 hours. Feldman (*Trans. Stud. Coll. Phys. Phila*, 1946, **14**, 81) showed that " systems of dosage with streptomycin in guinea-pigs, involving short or long intervals and either continuous or intermittent, had an essentially equal efficacy ". The present author suggests that these findings can be explained by assuming that a single adequate dose of streptomycin, producing a blood and tissue concentration of 30 μg. per ml. or more, does in fact kill a substantial proportion of the actively multiplying and accessible bacilli in the body. It will then be several days before those which are inaccessible in foci of necrosis or frank caseation are able to resume the invasion of surrounding tissues. This hypothesis on the bactericidal effect of streptomycin would account for the success of intermittent treatment, which has been shown to have the further advantage that it delays the emergence of resistance.

Kenneth Marsh

2140. **Primary Streptomycin-resistant Tuberculosis in a Newborn Child. Simple Method of Assessing Streptomycin Resistance**

J. E. TINNE and J. L. HENDERSON. *Lancet* [*Lancet*] **2**, 901–904, Dec. 30, 1950. 4 figs., 7 refs.

The authors briefly review the litereature concerning the development of resistance to streptomycin by some strains of *Mycobacterium tuberculosis*, and emphasize the desirability of routine testing for streptomycin sensitivity before the start of treatment, owing to the possible presence of a streptomycin-resistant strain before treatment is started. The case history is given of miliary tuberculosis in a female infant aged 11 weeks, treated with 11·6 g. of streptomycin over 12 weeks, and which died 14 weeks after admission. One positive culture of *Myco. tuberculosis* was obtained at the start of treatment, and one near the end.

A streptomycin-sensitivity test by a vertical diffusion method is described. After sterilization, the water of condensation is removed from slopes of Lowenstein-Jensen medium and is replaced by 1 ml. of streptomycin solution of 1 μg., 10 μg., or 100 μg. per ml. concentration. The material to be cultured is then concentrated and inoculated on each slope. The test is carried out in duplicate with a control. The slopes are incubated in a vertical position up to 6 weeks. The authors tested 7 different strains by this method, including the two isolated from the patient. With 5 strains it was found that after 4 weeks' incubation there was a zone of inhibition, up to 1·75 cm. with the 1 μg. per ml. slope, up to 3·5 cm. with the 10 μg. per ml. slope, and complete inhibition with the 100 μg. per ml. slope. After 5 weeks a very few colonies began to appear in the zone of inhibition, mostly at the upper margin. These colonies were shown to be resistant by testing the streptomycin solutions, which were shown to have remained active. After 6 weeks these 5 strains showed up to 9 resistant colonies on the 10 μg. per ml. slope and up to 3 colonies on the 100 μg. per ml. slope. In the case of the strain isolated from the patient at the start of treatment, 55 resistant colonies appeared on the 100 μg. per ml. slope after 6 weeks' incubation, whereas with the strain isolated after 3 months' treatment the colonies on the 100 μg. per ml. slope were uncountable. The authors recommend the addition of a streptomycin antagonist to the medium when culturing material for tuberculosis from patients treated with streptomycin. They add 2 mg. of cysteine hydrochloride to every ml. of Lowenstein–Jensen medium before sterilization.

A. G. S. Heathcote

2141. **The Effect of Streptomycin on Tuberculous Meningitis. A Study of Three Cases at Necropsy**

M. G. NETSKY, N. S. RITTER, and H. M. ZIMMERMAN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 586–593, Dec., 1950. 12 figs., 8 refs.

Necropsy findings are described in 3 cases of tuberculous meningitis in which streptomycin had been given intramuscularly and intrathecally. The most striking finding was the almost exclusive limitation of fibrosis and minimal exudation in the leptomeninges of the spinal cord. This was in contrast with an active process of exudation and necrosis in the meninges of the brain stem and cerebrum. It is suggested that the higher concentration of streptomycin in the spinal meninges was responsible for the healing.

Kenneth Marsh

2142. **Adjuvants to Streptomycin in Treating Tuberculous Meningitis in Children**

I. A. B. CATHIE and J. C. W. MACFARLANE. *Lancet* [*Lancet*] **2**, 784–789, Dec. 16, 1950. 1 fig., 25 refs.

A series of 40 children with tuberculous meningitis were treated at the Hospital for Sick Children, Great Ormond Street, London, with streptomycin in combination with one or more forms of adjuvant therapy. The auxiliary drugs used were *p*-aminosalicylic acid, streptokinase, and " sulphetrone " (solapsone), and ventricular drainage was carried out in a number of cases requiring reduction of intracranial pressure. Streptomycin, in

the dosage recommended by the Medical Research Council (*Lancet*, 1948, **1**, 582), was given by the intrathecal route daily for a fortnight, every other day for a fortnight, and every third day for a further fortnight, making a total of 24 intrathecal injections over a period of 6 weeks. The drug was also given continuously for 6 months by intramuscular injection. Streptokinase (the streptococcal fibrinolysin which is capable of dissolving the exudate which forms at the base of the brain in meningeal tuberculosis) was added to the streptomycin solution and given to all 40 patients at each intrathecal injection. Sulphetrone, in doses of 0·05 to 0·1 g., was added to the streptomycin–streptokinase mixture in 34 cases. Signs of increased intracranial tension were present in 25 patients, and the pressure was relieved by inserting catheters into the lateral ventricles. In addition, *p*-aminosalicylic acid was given concurrently by mouth.

Of the 40 patients treated according to the above schedule 23 recovered, 19 following a single course of 24 intrathecal injections, 3 after a second 6-week course, and 1 after a 6-month course. The survival rate (58%) greatly exceeded that obtained in an earlier series of 20 children who were treated with streptomycin alone, of whom only 5 (25%) recovered. The authors ascribe the reduction in mortality to the use of the adjuvants, especially streptokinase. They believe that the lytic action of this agent on the fibrinous exudate reduces the risk of the development of hydrocephalus and of changes resulting from increased intracranial pressure. This premise is supported by the observation that all but one of the 20 children in the first series (treated with streptomycin alone) showed signs of increased pressure; similar signs were present in only 25 (62%) of the patients given streptokinase. The authors have deferred judgment on the value of sulphetrone, but are of the opinion that it is probably not of great value.

[This is an important paper which should be consulted in the original for fuller detail.] *G. B. Forbes*

2143. **Haemolytic Manifestations and Blood and Marrow Examinations in Sardinian Children during Treatment with *para*-Aminosalicylic Acid (PAS).** (Manifestazioni embolitiche ed esami ematomidollari in bambini sardi durante il trattamento con il " PAS ")
E. Depperu and M. Riccardi. *Pediatria* [*Pediatria*] **58**, 184–197, March–April, 1950. 4 figs., 19 refs.

The authors, working at the University of Sassari, observed haemolytic-like changes in the blood of 2 children during treatment for tuberculous meningitis with *p*-aminosalicylic acid (PAS). Five other children suffering from resolving tuberculous disease were given PAS in order to study the blood and bone-marrow changes. The patients' ages ranged from 2 to 9 years, and the dosage of PAS from 3 to 5 g. a day for 7 days, the blood and marrow examinations being carried out both before and after treatment. No other form of treatment was given during this period.

The blood haemoglobin level remained normal in 2 cases, but fell by 5% to 12% in the other 3. There was no appreciable change in the erythrocyte count, but there was a slight decrease in the number of leucocytes, the differential count showing a constant increase in the neutrophil granulocytes and a decrease in the number of lymphocytes. The reticulocyte count showed no significant change, but the fragility of the erythrocytes was slightly increased. The haematocrit findings showed no important change, Capps's index was unaltered, and the mean corpuscular diameter remained between 8 and 8·4 microns except in one case in which there was a slight decrease. In every case the direct Van den Bergh reaction was negative, but the indirect reaction was positive in all cases until 8 days after the cessation of treatment. Urobilinuria was observed in each case up to the 11th day. Bone-marrow examinations indicated an increase in erythropoiesis with an increase in the number of mature forms and a low leuco-erythropoietic rate. The percentage of myelocytes was higher than that of metamyelocytes. These changes appeared to be more marked in those patients who had haematological disorders, such as anaemia and abnormal erythrocyte fragility, before administration of PAS. *E. R. Cole*

2144. **The Treatment of Various Forms of Pulmonary Tuberculosis in Children with *para*Aminosalicylic Acid and its Sodium Salt.** (La terapia con acido *para*-aminosalicilico ed il suo sale sodico in alcune forme di tbc. polmonare infantile)
U. Pellegrini and G. Maini. *Lattante* [*Lattante*] **21**, 1–41, Jan., 1950. 21 figs.

Of 20 cases of pulmonary tuberculosis treated with *p*-aminosalicylic acid (PAS) or its sodium salt, 10 were of exudative type, 8 in the active lymph-node stage with toxic symptoms, and 2 were miliary cases, in one of which meningitis had developed. The last two were also treated with streptomycin. The Mantoux test was positive in each case. The patients had been febrile for not less than 8 and not more than 30 days and were all very ill and toxic, with anorexia, asthenia, pallor, and profuse sweating. Treatment with PAS was instituted as soon as clinical, radiological, and laboratory diagnosis was complete. The majority of patients received the sodium salt, and treatment was continued for 40 to 80 days, in dosages of between 0·4 and 0·5 g. per kg. body weight per day, divided into 8 three-hourly doses. In some cases it was possible to control the temperature, so that ambulatory treatment could be given. Ages varied from 1½ to 10 years.

A detailed history of each case is given, and the results are summarized in tabular form. In 16 cases the clinical result was good and in 4 mediocre [the terms are not defined], 17 improved radiologically, while 3 remained unchanged. In every case weight was increased and the erythrocyte sedimentation rate (E.S.R.) had diminished at the end of treatment. With the exception of the two miliary cases temperatures were reduced in an average of 4·1 days. In the 2 miliary cases temperature fell after 14 and 20 days respectively.

The authors conclude that PAS and, in particular, its sodium salt are well tolerated by children and have no apparent toxic effects even in large doses, either local or general; in the exudative and allergic phases of pulmon-

ary tuberculosis in children, though PAS produces a rapid fall in temperature and reduces the E.S.R., it does not seem to cause a parallel improvement in the actual lesion, which only seems to heal slowly after repeated courses of the drug; in cases in which pulmonary tuberculosis follows a more severe course (miliary or meningitic) PAS or its sodium salt should be used in combination with streptomycin. *E. R. Cole*

2145. **Febrile Reactions to *para*-Aminosalicylic Acid.** (Les poussées fébriles du P.A.S.)
B. KRIES, A. LIBERT, F. PAQUELIN, and J. ABRIC. *Presse Médicale* [*Pr. méd.*] **58**, 1285–1287, Nov. 18, 1950. 6 figs., 7 refs.

Rashes are not an uncommon occurrence during treatment with *para*-aminosalicylic acid (PAS). In the cases here described, however, 8 patients who were receiving PAS developed fever without a rash. In 7 the fever disappeared as soon as the PAS was discontinued, but in one case the temperature remained raised for 11 days. Skin tests with PAS were negative, but the fever returned each time its administration was resumed.
J. R. Bignall

2146. **The Bacteriostatic Activity of 4-Amino-5-iodosalicylic Acid against the Tubercle Bacillus; Early Results of its Therapeutic Use in Pulmonary Tuberculosis.** (L'attivita batteriostatica dell'acido 4-amino-5-jodosalicilico (JPAS) verso il bacillo di Koch e primi risultati nella terapia della tubercolosi polmonare)
G. PALERMO. *Riforma Medica* [*Rif. med.*] **64**, 1335–1338, Dec. 9, 1950. 2 figs., 6 refs.

A drawback in the treatment of tuberculosis with *para*-aminosalicylic acid (PAS) is its rapid excretion. The author has studied an iodine derivative of PAS which may be excreted more slowly. The compound investigated was found to be bacteriostatic in the test-tube [no figures are given, nor any comparison with PAS]. It is very toxic for guinea-pigs, and on this account the author was unable to get experimental evidence of its activity *in vivo*. In the human being, confirmation was obtained of its slow excretion: excretion rose slowly to the 7th hour after administration, then remained slightly below that level for the next 10 hours, then fell rapidly. In 20 patients with advanced pulmonary tuberculosis some clinical improvement was noted, but no radiological change. *M. Daniels*

2147. **Clinical Pathology of the Gastro-intestinal Tract in Pulmonary Tuberculosis.** (Клиническая патология желудочно-кишечного тракта больных туберкулезом легких)
D. A. MANUCHARJAN. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 6, 11–20, Nov.–Dec., 1950. 2 refs.

The author draws attention to the fact that the study of gastro-intestinal pathology in pulmonary tuberculosis has been sadly neglected. He examined 154 patients with pulmonary infections, sent to him for special investigation, and discovered that 10% suffered from tuberculosis of the gastro-intestinal tract, 3% from tuberculosis of the mesenteric lymph nodes, and 3% from chronic non-tuberculous gastro-enteritis. He also found that some patients suffered from gastric hypotonia and retarded digestion, which he attributes to the toxic effect of the tubercle bacilli on the muscular layer of the stomach. He hopes that improvements in the technique of radiological examination of the gastro-intestinal tract will be made to enable pre-ulcerative changes in the gastro-intestinal tract to be diagnosed. The author insists that a thorough physical, bacteriological, and radiological investigation of the gastro-intestinal tract should be made in every case of pulmonary tuberculosis, irrespective of whether there are any abdominal symptoms. *H. W. Swann*

2148. **Combined Treatment of Patients with Laryngo-pulmonary Tuberculosis.** (О комплексном лечении больных гортанно-легочным туберкулезом)
M. S. BINSHTOK. Проблемы Туберкулеза (*Probl. Tuberk.*] No. 6, 21–25, Nov.–Dec., 1950.

The treatment of advanced ulcerative forms of laryngeal tuberculosis associated with pulmonary tuberculosis by a combined method at a sanatorium on the shores of the Crimea has produced remarkable results. The essence of the treatment consists in giving small doses of streptomycin (5 to 20 g.) in association with *x*-ray therapy, electrocauterization, and other methods which will stimulate the resisting powers of the patient. An important part of the treatment is the *x*-ray therapy of the nervous system around the neck. The patients must be kept out of doors continuously, day and night. Immediate positive results of this combined treatment were obtained in 99% of cases, and clinical healing of the laryngeal tuberculosis occurred in 53·7% . During one year of observation 71% of 68 patients either returned to work or did not have any exacerbations and did not require further treatment for the larynx.
H. W. Swann

2149. **Collapse Therapy for Pulmonary Tuberculosis in Older Children.** (Коллапсотерапия при легочном туберкулезе у детей старшего возраста)
R. D. IVANITSKAJA. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 6, 29–34, Nov.–Dec., 1950.

Collapse therapy in pulmonary tuberculosis in older children is very effective; this is particularly true of treatment with artificial pneumothorax which is most effective in cases with signs of infiltration, especially during a primary infection. Artificial pneumothorax should be used more extensively and much earlier than is usually the case. Bilateral artificial pneumothorax should also be used more extensively as the results are as good as with a one-sided artificial pneumothorax. A frequent complication is pneumopleurisy, but children get over this much more easily than adults; usually there is no rise in temperature and the condition clears up in 1½ to 2 months. The exudate must be aspirated and replaced by air. It usually appears in children during the first 6 months after the induction of an artificial pneumothorax. Infiltration of the phrenic nerve with alcohol is not as effective in children as it is in adults, the paresis of the diaphragm being very short-lived.

Children tolerate a pneumoperitoneum very well, but it should be continued for a considerable time. The author recommends a combination of alcohol infiltration of the phrenic nerve with pneumoperitoneum.

H. W. Swann

2150. **Refill Pressure after Pneumolysis.** (Zur Frage des Druckes bei der Lüftfullung von Pneumolysehöhlen) E. H. MÜLLER. *Tuberkulosearzt* [*Tuberkulosearzt*] **5**, 15–21, Jan., 1951. 6 refs.

It is generally accepted that the maintenance of adequate collapse in extrapleural pneumothorax necessitates the creation of a positive pressure. Some authors recommend final pressures up to +40 cm. of water, while others find a final pressure of +5 to +10 cm. sufficient. The present author investigated this problem by systematically measuring the pressures in cases of extrapleural pneumothorax at certain intervals after refilling. He confirmed the finding of Kivikanervo that a high positive final pressure after a refill soon falls. The following tests were carried out: (1) In 4 patients who were left with a final pressure of +30 to +35 cm. of water the needle was kept *in situ*, connected with the manometer but clamped off. Pressures were read every 10 minutes for 2 hours with results as follows: after 10 minutes +13 to +17 cm.; after 30 minutes +10 to +15 cm.; after 2 hours +4 to +10 cm. (2) Six patients were left with a final mean pressure of +30 cm. of water. The pressure readings after 2 and 24 hours were +2 to +10 cm. and zero respectively. (3) Three patients were given refills with a final mean pressure of +40 to +44 cm. of water. Mean pressures after 24 hours were about 0 and +6 cm. respectively. Following the 24-hour reading a second refill was given with final pressures of about +20 cm. only. Mean pressures after another 24 hours were again between +5 and 0 cm. This shows that the higher the refill pressure, the steeper the fall, and that however high the final pressure may be after a refill, the pressure will adjust itself quite as quickly to a level near zero as in cases left with a low positive pressure. (4) In 4 patients with a final mean refill pressure of +20 cm. who showed, after 24 hours, a mean pressure of zero or slightly below, further pressure readings 2, 3, and 8 days after the refill showed hardly any further fall.

It is concluded that during the first days after operation there is considerable permeability of the thoracic wall and frequent refills are required. After the wound surface is covered by a fibrinous membrane the rate of absorption and diffusion of gas depends on the pressure rather than on the thickness of the thoracic wall (or of the extrapleural lung cover). It is therefore impossible to maintain a high positive pressure within the extrapleural cavity for any length of time, as absorption and diffusion are only accelerated with increasing pressure. Once a pressure equilibrium has been reached and the pressure has dropped nearly to zero, further gas diffusion is very slow. It is thus not only useless but quite unnecessary to create, and to try to maintain, a high pressure in extrapleural pneumothorax in order to keep the lung adequately collapsed. Regular *x*-ray control is the best guide to the timing of refills, which should depend on the tendency of the lung to re-expand rather than on the pressure. High positive pressure cannot prevent re-expansion or creeping-up of the lung in an obliterating pleural space following effusion and infection. [This, of course, also applies to refills of intrapleural pneumothorax.] *E. G. W. Hoffstaedt*

2151. **Clinically Silent Tuberculous Foci in Bone.** (Klinisch stumme Tbk.-Herde im Knochen) H. KEPPEL. *Tuberkulosearzt* [*Tuberkulosearzt*] **5**, 40–42, Jan., 1951.

Randerath found latent foci in the skeleton in over 80% of necropsies on patients who died from pulmonary tuberculosis. The author observed in 871 patients with active pulmonary tuberculosis 51 cases (5·85%) with clinically and radiologically manifest skeletal tuberculosis. Two cases are described of unilateral clinical tuberculosis of the knee-joint in children where the control *x*-ray of the " healthy " knee revealed latent foci in the femoral condyle near the epiphyseal line. After clinical observation for 1 and 2 years respectively, complete healing of the latent foci had taken place without ever producing any clinical signs or symptoms. It is open to conjecture how far the general treatment and the immobilization of the diseased limb may have contributed to the symptomless healing of the latent foci. These observations, however, provide additional support for the concept of tuberculosis as a generalized, systemic disease rather than an isolated, localized lesion in the surgical sense.

[These cases also show that the secondary stage of the disease may produce several haematogenous foci anywhere in the body. Though the vast majority of these secondaries remain silent throughout life, any serious lowering of the general or of the organ resistance, such as an injury to a limb or to the chest, can activate such a silent focus and may produce signs and symptoms of manifest tuberculosis after an " incubation " (or, rather, latency) period of some weeks, if not months.]

E. G. W. Hoffstaedt

2152. **Primary Cavitation and Bullous Pseudo-cavitation of the Lung in Infancy and Adolescence.** (Les cavernes primaires du poumon et les images bulleuses pseudo-cavitaires chez l'enfant et l'adolescent) J. BRUN and J. DUMAREST. *Pédiatrie* [*Pédiatrie*] **4**, 9–42, 1950. 4 figs., bibliography.

The authors have based their study on reports published in both French and foreign journals and on a series of 23 cases of primary cavitation which they observed in children and adolescents at the Tuberculosis Clinic, the Jules–Courmont Hospital, and Infant Medical Clinic at Lyon, and at the Roe de Fiz Sanatorium.

They found that the excavation of the primary focus usually follows 2 to 6 months after the allergic phase either in a healthy parenchyma or in a caseous area, the cavity appearing in the middle or lower zones of the lung. Clinical and radiological findings vary, depending largely on the initial clinical picture together with any complications that may develop later. A distinction must be drawn on the one hand between isolated primary

cavities which are of limited symptomatic significance, appearing as a clear round area and varying in size during evolution, and on the other hand the cavities situated in the centre of infiltrations and usually detected tomographically. Efforts should be made to find the organisms by gastric lavage. The progress of these lesions is variable but usually benign, unlike those of tertiary phthisis. It is important to institute collapse therapy to ensure a rapid and certain recovery and obviate complications due to local or general dissemination. Radiological and clinical diagnosis is often difficult, especially with the bullous pseudo-cavities of emphysematous or bronchiolar origin. These shadows may appear in a healthy parenchyma, but are usually obscured by opacities, either secondary to dissemination from a focal breakdown or as a result of atelectasis, epituberculosis, or bronchostenosis. They may be distinguished from primary cavities because of their sudden appearance, their variability in volume, spontaneous evolution after a short period, and negative radiological findings. The relationship between tuberculous lesions and those of bullous emphysema must, however, be borne in mind.

Confusion may arise from shadows of lymph nodes, which are rarely seen in infants, but the most careful consideration should be given to the tertiary tuberculous cavity in infants who have been in the allergic phase for a long time, as the prognosis is much more sombre in these cases than in primary cavitation. Many primary cavities are produced as a result of repeated exogenous infections, but other pathogenetic factors are often involved. Streptomycin should not be used as a routine, but should be reserved for the more serious cases and for infants. *E. R. Cole*

2153. **Permanence of So-called Temporary Phrenic Nerve Paralysis**

H. H. Seiler and J. D. Murphy. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **63**, 81–84, Jan., 1851. 7 refs.

This report summarizes an analysis of 288 patients subjected to phreniclasia (335 operations) for temporary phrenic nerve paralysis, in an effort to determine the permanence of the resulting paralysis. The observations in 288 patients indicated the occurrence of some degree of permanent paralysis in approximately one-half of the cases and total loss of diaphragmatic function in almost one-fifth.—[Authors' summary.]

2154. **Antigenic Activity of Fresh, Frozen, and Dry BCG Vaccine**

K. Birkhaug. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **63**, 85–95, Jan., 1951. 2 figs., 7 refs.

Glucose B.C.G. vaccine sustains a greater loss of living organisms during the prolonged process of drying from the frozen state than during the quick process of simple freezing as an alternative means of preservation. Dry glucose B.C.G. vaccine retains its surviving organisms at a relatively stable numerical level for one year when kept at 2° to 4° C., while frozen glucose B.C.G. vaccine gradually dissipates its living organisms to a lower numerical level than the dry vaccine when kept at −20° C. for one year.

The morphologic, cultural, and biologic characteristics of surviving one-year-old dry and frozen B.C.G. remain unaltered from those possessed by fresh liquid vaccine. The antigenicity of one-year-old dry glucose B.C.G. vaccine is lower than that of fresh liquid vaccine. Moreover, the one-year-old frozen glucose vaccine is weaker antigenically than similarly aged dry glucose vaccine as demonstrated by skin lesions, tuberculin sensitivity, and resistance against a challenge infection with virulent tubercle bacilli.

By quadrupling the multiple skin punctures, the use of one-year-old vaccine, either the dry glucose B.C.G. vaccine or the frozen glucose vaccine, produces a degree of resistance against a challenge infection with virulent tubercle bacilli comparable to that stimulated by one-fourth the number of skin multiple punctures and the use of fresh liquid vaccine.

With adequate adjustment of multiple skin punctures and dosage with reference to living organisms or repeated inoculations, the use of one-year-old and completely controlled dry or frozen B.C.G. vaccine should prove just as effective as the use of fresh liquid vaccine. Moreover, the dry or frozen vaccine seems preferable to fresh liquid vaccine because the latter preparation is incompletely controlled, and maintains optimal antigenic activity for only 10 days after its preparation.—[Author's summary.]

2155. **Hyaluronidase in Tuberculosis**

H. J. Corper and M. L. Cohn. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **63**, 108–115, Jan., 1951. 3 figs., 11 refs.

An investigation has been made of the effects of the enzyme hyaluronidase on the spread of tuberculosis in guinea-pigs infected by injection of tubercle bacilli intracutaneously, subcutaneously, and intravenously. It was found that hyaluronidase injected intracutaneously at the site of intracutaneous injection of tubercle bacilli, together with, or one hour after, injection of the bacilli exerts a marked spreading effect on the bacillary suspension, resulting in the development of multiple skin tubercles as well as more extensive ulceration.

Subcutaneous injection of hyaluronidase, 25 units daily for 30 days in guinea-pigs, exerted no appreciable effect on the generalized tuberculosis resulting from subcutaneous or intravenous injection of virulent human tubercle bacilli. These experiments corroborate earlier observations on spreading effects on tuberculosis of less pure agents, such as testicular extracts, *Staphylococci*, and *Streptococci*, which contain or form hyaluronidase.

It is conceivable that hyaluronidase can be used efficiently under certain circumstances to aid penetration of therapeutic agents into disease foci with beneficial results. It does not seem advisable, however, to use hyaluronidase to speed entrance of therapeutic agents into disease foci, such as those in tuberculosis, when these agents are incapable of destroying the bacilli readily. (For example, streptomycin, even 1,000 γ per c.c. in contact *in vitro* for 3 months, does not destroy the viability

of tubercle bacilli.) Thus, local spread of the bacilli and disease foci may result, as occurred in the experiments recorded here.—[Authors' summary.]

2156. **The Accelerated Biological Method for Diagnosis of Tuberculosis by means of Testicular Hyaluronidase.** (Rozpoznawanie gruźlicy przyśpieszoną metodą biologiczna za pomoca hialuronidazy jadrowej)
B. ZABLOCKI and H. KOLSUT. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **5**, 1252–1254, Sept. 4, 1950. 3 refs.

The authors describe their investigations on the biological method for the diagnosis of tuberculosis, in which they compared the results obtained by injection of two lots of guinea-pigs with tuberculous material with and without the addition of hyaluronidase.

The addition of hyaluronidase is said to present the following advantages: (1) a shortening of the time for the enlargement of the inguinal lymph nodes by 10 days (22 days in controls); (2) a shortening of the time of formation of fistula at the site of inoculation by 19 days (36 days in controls); (3) a shortening of the time of observation of the inoculated guinea-pigs by 3 weeks. Post-mortem examination of guinea-pigs inoculated with tuberculous material to which hyaluronidase was added yielded positive results on the average about 22 days after inoculation. The addition of hyaluronidase to the injected material is of special value in cases in which tubercle bacilli may be very scanty, as in the cerebrospinal fluid, milk, or exudates.

The method is as follows: 1 ml. of the concentrated material for examination is homogenized with 4% solution of sodium hydroxide (for 20 minutes at 37° C.), and then neutralized and mixed with 1 ml. of 8% emulsion of the testicular hyaluronidase made in sterile isotonic saline. In controls 1 ml. of saline is used instead of the emulsion of hyaluronidase. In each case the guinea-pigs are inoculated subcutaneously in the inguinal region. *J. W. Czekalowski*

2157. **The Bactericidal Effect of Surface-active Agents on Tubercle Bacilli**
C. R. SMITH, H. NISHIHARA, F. GOLDEN, A. HOYT, C. O. GUSS, and M. C. KLOETZEL. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65** 1588–1600, Dec. 1, 1950. 18 refs.

A total of 142 representative surface-active agents, including the anionic, cationic, and nonionic groups, were tested for bactericidal action against tubercle bacilli. One preparation, "armeen 14D", showed sufficient activity to be considered for practical disinfection. Its precise usefulness, however, awaits further study. As a group, the surface-active agents are not good disinfectants against the tubercle bacillus. This applies even to the quaternary ammonium salts, which are now in widespread use in disinfection and sanitation. —[Authors' summary.]

2158. **A Comparative Study of Tuberculosis Mortality Rates**
V. H. SPRINGETT. *Journal of Hygiene* [*J. Hyg., Camb.*] **48**, 361–395, Sept., 1950. 20 figs., 39 refs.

LEPROSY

2159. **Is there a New Disease due to Acid-fast Bacilli in Africa? Preliminary Note.** (Faudra-t-il tenir compte d'une nouvelle affection à bacilles acido-résistants en Afrique? Note préliminaire)
E. VAN OYE and M. BALLION. *Annales de la Société Belge de Médecine Tropicale* [*Ann. Soc. belge Méd. trop.*] **30**, 619–627, Sept. 30, 1950. 1 fig., 6 refs.

In 1948 MacCallum and his colleagues in Australia described a new disease characterized by ulcerations of the extremity due to an acid-fast bacillus which is distinct from the tubercle and leprosy bacilli (*J. Path. Bact.*, 1948, **60**, 93). Evidence is now brought forward of a similar disease in the Belgian Congo: a rapidly spreading ulcer involving the dorsum of the foot in a boy of 6½ years. No form of treatment had any effect on the ulcer. It was stated in the discussion that similar cases had been seen in Haut-Ituri as long ago as 1942. [The cultural characteristics of the bacillus are not described.]
G. M. Findlay

2160. **"*Cimédone*" in the Treatment of Leprosy.** (Sur le cimédone dans le traitement de la lèpre)
J. FERON. *Bulletin de la Société de Pathologie Exotique* [*Bull. Soc. Path. exot.*] **43**, 658–662, 1950. 9 figs.

From November, 1949, to May, 1950, 20 lepers were treated with solapsone (sulphetrone; referred to in France as "*cimédone*" or "RP 3668"); 16 had lepromatous lesions, 3 nerve lesions, and one had a mixed form. A dose of 0·5 g. was given daily for 6 days a week. In the patients with nerve lesions there was no change and in the patient with mixed lesions the anaesthetic patches showed no improvement. All the patients with lepromatous lesions were greatly benefited, even those in whom the disease was of very long-standing; 3 relapsed. Almost all lepers suffer from signs of food deficiency and ample amounts of all the B-vitamins should be provided. *G. M. Findlay*

2161. **Treatment of Leprosy by Thiosemicarbazone (T.B.I). Results of the First 11 Months' Observations.** (Traitement de la lèpre par le thiosémicarbazone (T.B.I). Résultats d'une première expérimentation de 11 mois)
J. SCHNEIDER, P. LAVIRON, L. LAURET, and A. BASSET. *Bulletin de la Société de Pathologie Exotique* [*Bull. Soc. Path. exot.*] **43**, 733–739, 1950. 2 figs., 2 refs.

Thiacetazone (also known as thiosemicarbazone, "T.B.I", or "conteben") was first used by Hohenner (*Med. Klinik.*, 1949, **43**, 1378) in the treatment of leprosy. The present authors began to use it in September, 1949. In all, 14 patients with the lepromatous type of disease have been treated for 3 to 11 months and have shown very considerable improvement in the lesions, although acid-fast bacilli are still present in the nose. The dosage was 100 mg. daily for the first week, 150 mg. daily for the second week, and thereafter 200 mg. weekly. The drug was taken by mouth 6 days weekly without any rest periods. The only toxic results were slight headache and albuminuria. Lepra reactions were mild and did not call for cessation of treatment. *G. M. Findlay*

2162. **A Critical Review of the Present Position of Sulphone Therapy in Leprosy**
R. G. COCHRANE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **44**, 259–270, Dec., 1950. 7 refs.

After reviewing the relative values of hydnocarpus therapy and the various sulphones hitherto used, the author contends that bi-weekly intramuscular injections of 2 ml. of a 50% aqueous solution of sulphetrone is the safest and most effective treatment for general use. Unless it can be shown that 0·4 g. of 4 : 4′-diaminodiphenylsulphone weekly, or even a smaller dose, is effective, that drug has no advantage but cheapness, and even that consideration is outweighed by the need to give iron and yeast on account of its blood-destroying properties.

In institutions daily oral administration of tablets is troublesome, especially if repeated blood examination is necessary, and ambulatory treatment with toxic tablets may lead to difficulties. The author concludes that sulphone therapy, particularly in advanced lepromatous cases, will in the great majority of cases prevent or alleviate the distressing eye and throat symptoms and render an increasing proportion of cases negative.

Clement Chesterman

2163. **Diaminodiphenylsulphone in the Treatment of Leprosy**
J. LOWE. *Lancet* [*Lancet*] **1**, 18–21, Jan. 6, 1951. 5 refs.

The author reports on the dosage used and toxic effects observed in the treatment of more than 500 cases of leprosy among Africans with diaminodiphenylsulphone (DADPS). For general use in Nigeria, where constant medical supervision is often not possible, two methods of administration are recommended, one on 6 days a week with daily doses of 100 mg. for the first 6 weeks, then rising to 200 mg. a day, and the other twice weekly (with doses starting at 100 mg. and rising by steps of 100 mg. each week to 400 mg. in the fourth week, this dosage to be maintained, if possible, as long as treatment lasts. This dosage is somewhat less than that initially used, but it does not appear to be appreciably less effective.

The toxic effects observed were of the same type as those encountered with other sulphones. There was an initial anaemia usually lasting a few weeks, and then the haemoglobin level became stabilized at about 11 g. per 100 ml. The administration of iron in the form of ferrous sulphate helped considerably in the maintenance of the haemoglobin level. The gradual induction of treatment reduces the incidence and degree of serious anaemia. About 2% of the patients developed a general dermatitis due to sensitization: unless the drug is stopped this dermatitis may proceed to exfoliation, and may even be fatal. The striking feature about the dermatitis was that it appeared in the first few weeks of treatment or not at all. Attention is drawn to the occurrence of psychological disturbances during sulphone treatment, 6 cases being described in detail among one group of 350 patients (although in another group of 200 cases no psychosis had occurred). A psychotic background was present in 4 of the cases. These reactions seem to be more common and severe during treatment with DADPS, than with "sulphetrone". Erythema nodosum leprosum was common during sulphone therapy, developing in about 30% of lepromatous cases at some time during treatment. The injection of antimony preparations was found to be helpful in treating this condition.

R. Wien

2164. **Haemolytic Anaemia during Treatment of Leprosy with Diaminodiphenylsulphone by Mouth. Report of a Case**
K. RAMANUJAM and M. SMITH. *Lancet* [*Lancet*] **1**, 21–22, Jan. 6, 1951. 3 refs.

The case is reported of a male Indian, aged 36, who had had leprosy for 3 years. He was given 100 mg. daily of diaminodiphenylsulphone for 13 days, then 200 mg. daily for 10 days, and 300 mg. daily for the next 13 days. On the 35th day of treatment the patient complained of nausea, weakness, and fever. The urine gave a strongly positive reaction to the Schlesinger test for urobilin, and methaemalbuminaemia, bilirubinaemia, and a decrease in erythrocyte count and haemoglobin level were observed.

R. Wien

2165. **The Initial Manifestations of Leprosy as Observed in Contacts.** (Manifestaciones iniciales de la lepra; observadas en convivientes)
L. A. PITT and C. A. CONSIGLI. *Actas Dermo-Sifiliográficas* [*Actas dermo-sifiliogr., Madr.*] **42**, 3–11, Oct., 1950. 8 refs.

2166. **Epithelioma Supervening on a Leproma.** (Epitelioma sobre leproma)
X. VILANOVA, M. LLORENS RIBAS, and L. ALVARADAO. *Actas Dermo-Sifiliográficas* [*Actas dermo-sifiliogr., Madr.*] **42**, 39–43, Oct., 1950. 2 figs.

SPIROCHAETAL INFECTIONS

2167 (*a*). **Oral Aureomycin in the Treatment of Tropical Ulcers and Cancrum Oris**
O. AMPOFO and G. M. FINDLAY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **44**, 307–310, Dec., 1950. 2 refs.

A report is given on the treatment of 8 cases of tropical ulcer with aureomycin by mouth. All were in African children from the Gold Coast and the ulcers, which had been present for from 1½ to 3 months, were situated in the region of the ankle. No local treatment was given apart from the application of a piece of lint to keep away the flies. The dose of aureomycin usually given was 4 to 6 250-mg. capsules daily for 4 to 7 days, although 2 patients received only 3 capsules daily, and for 3 patients the treatment was continued for only 3 days. No untoward toxic effects were noted.

Spirochaetes and fusiform organisms were present in smears taken from the ulcers before treatment, but had disappeared in 5 cases after 24 hours, in 7 after 48 hours, and in all after 72 hours of treatment. All of the ulcers

were quite clean at the termination of treatment and proceeded to heal completely, there being no sign of relapse 6 to 12 weeks afterwards.

An additional case is described, of cancrum oris in a 3-year-old child, who had signs of marked ariboflavinosis with " crazy-pavement " skin, necrosis of the jaw, and loss of both upper central incisors. One 250-mg. capsule of aureomycin was given 3 times daily for a week to a total of 5·25 g. Spirochaetes and fusiform bacilli disappeared from the smears, a sequestrum separated on the fifth day, and the patient made an uneventful recovery. *R. R. Willcox*

2167 (*b*). **The Treatment of Yaws by Aureomycin**
O. AMPOFO and G. M. FINDLAY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **44**, 311–313, Dec., 1950. 12 refs.

The authors have previously reported the treatment of 3 cases of yaws with aureomycin (*Nature, Lond.*, 1950, **165**, 398). In the cases now described 6 African children with secondary yaws, one of whom had a yaws ulcer in addition, and a seventh child with yaws periostitis were all treated with 250 mg. of aureomycin given orally 3 times daily for 7 days. No toxic effects were noted. As it is usual in West Africa for yaws to be treated with intramuscular injections and the natives are convinced of their superiority over oral treatment, a daily intramuscular injection of 1 ml. of physiological saline was given in addition. The follow-up period ranged from 6 weeks to 6 months, and of 2 patients tested after 6 months the serum reaction for syphilis (Kahn) was found to be negative in one, and only doubtfully positive in the other. The advantages of an oral over an injection method of treatment in mass campaigns are pointed out. *R. R. Willcox*

2167 (*c*). **Chloramphenicol in the Treatment of Yaws and Tropical Ulcer**
O. AMPOFO and G. M. FINDLAY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **44**, 315–318, Dec., 1950. 8 refs.

The authors have already reported the successful treatment with aureomycin of cases of tropical ulcer and yaws (see Abstracts 2167 (*a*) and (*b*)). Their findings in cases treated with chloramphenicol are now reported. Three African children with tropical (phagaedenic) ulcers situated in the region of the ankle were given two 250-mg. capsules of chloramphenicol 3 times daily for one week. Numerous spirochaetes and fusiform organisms were found in smears taken from the ulcers before treatment; these disappeared within 48 hours and the ulcers all healed within 3 weeks of starting treatment. One patient developed an irritant erythematous rash on the third day, but treatment was not interrupted. Three other patients, whose ulcers also contained spirochaetes and fusiform bacilli before treatment, were given 2 g. of chloramphenicol daily in divided doses, morning and evening, for 4 days. The ulcers healed within 3 weeks in 2 cases, but in the third case healing took 35 days. During a follow-up of 2 months no recurrences were noted. [The potentialities of these oral antibiotics in the treatment of this disabling condition, which is widespread throughout tropical Africa, are enormous.]

In addition, 4 children with secondary yaws were given 10·5 to 21·0 g. of chloramphenicol over a period of 7 days. The lesions began to dry up within 48 to 72 hours and had all healed by the time that the treatment had been completed. Six weeks later the Kahn-test response was still positive, but observation continues. *R. R. Willcox*

2168. **Ghoul Hand**
D. B. JELLIFFE. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **53**, 238–240, Dec., 1950. 1 fig., 13 refs.

Ghoul hand is a form of keratotic vitiligo; it is usually symptomless and has a slow insidious onset. It is generally bilateral and occurs almost exclusively in males. The skin of the palms lacks pigment and is white or yellowish: the depigmentation often extends to the dorsum of the fingers and hand. Scattered areas of brownish hyperpigmentation are present on the pale skin. The palmar skin is greatly thickened, dry, inelastic, taut, and slightly translucent; the mobility of the hand is consequently reduced. Pain is uncommon. Twenty cases were examined in order to assess any connection with yaws. Signs of chronic yaws were present in 15, and 12 gave a positive past history. The Kahn test was strongly positive in all cases. Results of treatment with neoarsphenamine were difficult to assess, but 4 patients showed increased mobility of the hand. A similar condition of the soles was noted in 4 cases. The author believes that ghoul hand is probably due to tertiary yaws, and compares the lesion to the dyschromic skin lesions of chronic pinta. *W. H. Horner Andrews*

PROTOZOAL INFECTIONS

2169. **Radical Cure of Relapsing Vivax Malaria with Pentaquine–Quinine: a Controlled Study**
B. STRAUS and J. GENNIS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 1413–1422, Dec., 1950. 1 fig., 18 refs.

Earlier work on pamaquin is reviewed and the conclusion reached that a daily divided dose of 60 mg. together with 2 g. of quinine for 14 days was no certain cure of relapsing vivax malaria. Increasing the pamaquin dosage to 90 mg. produced gastro-intestinal and circulatory symptoms, cyanosis, T-wave changes in the electrocardiogram, and occasionally psychosis and coma. Alving and others obtained better results with 60 mg. of pentaquinine and quinine. A total of 50 cases of relapsing vivax malaria were treated with a course of pentaquine monophosphate, 10 mg., and quinine sulphate, 0·6 g., thrice daily for 14 days. In the follow-up period, varying from 6 to 18 months, only one patient suffered a relapse (on the 115th day).

Chosen alternately with the above, 49 cases served as a control and were treated with chloroquine diphosphate,

a total of 2·5 g. being given in 3 days. Of these, 17 relapsed. Toxic symptoms were negligible, though a fever up to 103·4° F. (39·7° C.) developed in 7 cases between the 7th and 11th day and subsided quickly without interruption of treatment.

It is claimed that eradication of vivax malaria was achieved in 98% of these cases with only half the previously recommended dosage of pentaquine.

Clement Chesterman

2170. **The Influence of the Genetic Constitution in the Resistance of the Mouse to Experimental Infection with *Trypanosoma cruzi*.** (Influencia de la constitución genética en la resistencia de la laucha a la infección experimental por *Trypanosoma cruzi*)

T. Pizzi, M. Agosín, R. Christen, G. Hoecker, and A. Neghume. *Biológica. Trabajos del Instituto de Biologia "Juan Noe"* [*Biológica. Trab. Inst. Biol. "Juan Noe", Chile*] Nos. 8–11, 43–53, 1948 (publ. 1950). 3 figs.

When different strains of mice are inoculated with *Trypanosoma cruzi* it is found that some strains are highly susceptible, whereas others are highly resistant. Statistically significant figures show that Rockefeller, Ay, Ak, and Daab strains have a high resistance, whereas A, Dba, C57, and C3H are highly susceptible. In the susceptible mice parasites are found in large numbers in the peripheral blood stream and the mortality is from 51 to 64%, whereas with the resistant strains mortality ranges from 4 to 20%.

G. M. Findlay

2171. **Experimental Infection of the Rabbit with *Trypanosoma cruzi*.** (Algunas caracteristicas de la infestación experimental con *Trypanosoma cruzi* en el conejo)

M. Agosín and O. Badínez. *Biológica. Trabajos del Instituto de Biologia "Juan Noe"* [*Biológica. Trab. Inst. Biol. "Juan Noe", Chile*] Nos. 8–11, 11–31, 1948 (publ. 1950). 18 figs.

The rabbit is less sensitive than other laboratory animals to infection with *Trypanosoma cruzi*. There are, however, nests of organisms in white and red muscular fibres which become elongated and show acute necrosis involving large segments. In addition macrophages from the interstitial tissues invade the nests of parasites when these nests come into contact with the surface of the muscle fibres. A similar reaction is not seen in other infections, and it is possibly related to the high resistance found in the rabbit.

G. M. Findlay

2172. **The Cattle Trypanosomiases: Cryptic Trypanosomiasis**

R. N. T.-W.-Fiennes. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 222–237, Oct., 1950. 14 refs.

Observations carried out in Kenya have convinced the author that in bovine trypanosomiasis primary infection of the blood is succeeded by a secondary stage of the disease in which the infection is cryptic, trypanosomes reappearing in the blood sporadically and in small numbers. This stage is associated with a morbid-tissue focus which, in the case of *Trypanosoma congolense*, may be represented by the adrenal cortex and the anterior pituitary glands; moreover, both this species and *T. vivax* have also been recovered from the pre-scapular lymph nodes. However, most of the evidence for cryptic trypanosomiasis is derived from (*a*) the demonstration of a specific antibody, (*b*) the results of prophylactic and subcurative drug treatment, and (*c*) the development of severe clinical symptoms in the absence of visible blood infection. This evidence is adduced in great detail in numerous tables.

The presence of antibodies in the serum of infected cattle after they ceased to show *T. congolense* in their blood was demonstrated by the protection it afforded to mice inoculated with various strains of this trypanosome (mouse-protection test). It was also shown that the serum protects the mice only so long as the infection in the bovines is latent (premunition), and not after their complete recovery.

Treatment of *T. congolense* infections with inadequate doses of "dimidium" and "antrycide" inhibited the primary type of disease for periods up to 4 months, mitigated its effects when it relapsed, and enabled the host to make a spontaneous recovery after a prolonged cryptic infection which was demonstrable by the mouse-protection test. The prophylactic administration of both these drugs, in *T. congolense* and *T. vivax* infections, had the effect of producing a cryptic infection, which in the case of dimidium was benign, but in the case of antrycide was in some cases fatal. Acute symptoms are therefore present not only in the primary disease but also in the secondary disease, but whereas in the former case they are associated with a blood infection, in the latter they appear to arise from a focus in the tissues. It was also shown that the characteristic anaemia of trypanosomiasis is common to both phases of the disease. Both cryptic infection and the state of premunition in cattle are regarded as manifestations of the secondary stage of trypanosomiasis.

C. A. Hoare

2173. **Serum Iron in Visceral Leishmaniasis.** (Il Fe serico nella leishmaniosi interna)

P. De Caprio. *Pediatria* [*Pediatria*] **58**, 170–176, March–April, 1950. 29 refs.

The author investigated the serum iron level in 21 children, whose ages ranged from 6 months to 6 years, suffering from visceral leishmaniasis before the institution of antimony treatment. The diagnosis was confirmed in each case by demonstration of the parasites in a bone-marrow smear taken by tibial puncture. In 11 cases the serum iron level was below normal, varying from 17 to 58 μg. per 100 ml., in 3 cases it was normal, and in 7 cases it was above normal, ranging from 129 to 282 μg. per 100 ml. These results do not compare with figures obtained by previous workers, and the author devotes the rest of his paper to a discussion of the parts played by the reticulo-endothelial system, the spleen, and the bone marrow in producing them. He concludes that the serum iron level in leishmaniasis depends on the combination of the effects of these three factors together with others as yet unknown.

E. R. Cole

AMOEBIASIS

2174. **Studies on the Influences of Intestinal Flora upon the Excystation of *Entamoeba histolytica in vitro*. III. On the Influences of Pure Strain of Bacteria upon the Excystation of *Entamoeba histolytica*. IV. Influences of Pathogenic Bacteria upon Excystation; General Discussion and Conclusion.** [In English]
K. ISHINO. *Kitasato Archives of Experimental Medicine* [*Kitasato Arch. exp. Med.*] **23**, 135–144, Oct., 1950.

This paper from the Department of Parasitology of the Keio-Gijuka University Medical School, Tokyo, records studies of the influence of bacteria on the excystation of *Entamoeba histolytica* in cultures. Cysts free from bacteria do not show any tendency to excystation. This is brought about by the addition of cultures of *Bacterium coli*, to a less extent by cultures of paracolon bacilli, and not at all by cultures of *Aerobacter aerogenes* or Gram-positive cocci. Excystation occurs more readily when four cultures of pure strains of bacteria are added than with the addition of one or two strains. The time necessary for excystation and the rate of excystation vary with the strain of cyst as well as with the accompanying bacteria. Media in which *Bact. coli* has grown does not cause excystation: it is the growth of the bacteria themselves which is responsible for the change. The serial subculture of amoebae with one pure strain of bacterium is not successful. *G. M. Findlay*

2175. **Biological Studies on *Endamoeba histolytica* IV. Direct Action of the Antibiotic, Prodigiosin**
W. BALAMUTH and M. M. BRENT. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 374–378, Nov., 1950. 4 figs., 19 refs.

Prodigiosin was extracted in the authors' laboratory from surface cultures of *Serratia marcescens* [*Bacillus prodigiosus*] grown on Hayes's medium adjusted to *p*H 6·7 and containing 1·5% agar. The cultures were harvested after 4 days' incubation in the dark at 23° to 25° C., and the pigment was extracted by the method of Wrede and Hettche (*Ber. dtsch. chem. Ges.*, 1929, **62**, 2678.) The properties of the substance, including the absorption characteristics, corresponded to those of the original. The action of this antibiotic was studied on two distinct strains of *Entamoeba histolytica*, the UC strain associated with a mixed bacterial flora, and the NRS strain associated only with *Aerobacter aerogenes*. The test medium was buffered egg-yolk infusion (*p*H 7·40) plus rice starch (Balamuth, *Amer. J. clin. Path.*, 1946, **16**, 380), 0·5 ml. of inoculum being added to 10 ml. of medium or 1·0 ml. to 30 ml. in different experiments. Amoebae in the inocula were counted on haemocytometers and exceeded 100,000 in all critical experiments. Yields were usually recorded after 48 to 72 hours as simply present or absent. From all apparently negative tubes bacterial counts were made and 0·2 ml. of sediment was subcultured into sterile medium for an additional 72 hours' incubation. Stock solutions of prodigiosin were maintained in ethanol and checked for sterility before use. Dilutions were prepared in the range 1 : 20,000,000 to 1 : 100,000, the control tubes receiving an equivalent concentration of ethanol.

The monobacterial NRS strain of *E. histolytica* proved the more susceptible, failing to survive in the presence of prodigiosin in a dilution of 1 : 400,000, while the UC strain failed to survive in the presence of 1 part of prodigiosin in 100,000, even with relatively huge inocula of amoebae. In neither case was the bacterial flora, oxidation–reduction potential, or *p*H adversely affected by the experimental treatment. The authors conclude that prodigiosin exerts a profound and direct action against *E. histolytica in vitro*. *Norval Taylor*

2176. **Experimental Infection of Guinea Pigs with *Endamoeba histolytica***
D. J. TAYLOR, J. GREENBERG, B. HIGHMAN, and G. R. COATNEY. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 817–828, Nov., 1950. 11 figs., 19 refs.

The inoculation of guinea-pigs with a strain of *Entamoeba histolytica*, which produced a fatal infection, is described from the U.S. National Institutes of Health. The strain had been previously used by Tobie (*Amer. J. trop. Med.*, 1949, **29**, 859) for the experimental infection of rabbits. Cultures of amoebae of this strain were injected directly into the guinea-pig's caecum at laparotomy.

Animals weighing less than 256 g. were successfully infected, but none weighing more than this were found to be infected. All animals dying before the 30th day after inoculation (99 out of 192 animals inoculated), and 15 other animals killed at various times, showed amoebic ulceration of the caecum, colon, and occasionally the rectum. Diarrhoea was generally observed 3 days before death, and was associated with lesions of the colon and rectum. The ulcers, which measured up to 10 mm. in diameter, extended into the mucosa, the submucosa, the muscularis, and the serosa, but did not undermine the adjoining mucosa. Some animals showed ulceration of deep glandular crypts extending into the lymphoid follicles lying in the submucosa, and one showed evidence of perforation of the intestinal wall. [These results are similar to those described previously by Carrera and Faust (*Amer. J. trop. Med.*, 1949, **29**, 647), except that in the present work the infections were often fatal. This was probably due to the higher pathogenicity of the strain used.] *R. A. Neal*

2177. **Laboratory Observations on the Actions of Aureomycin, Circulin, Polymyxins B, D, and E on *Endamoeba histolytica***
J. Y. C. WATT and W. B. VANDEGRIFT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 741–746, Nov., 1950. 12 refs.

The authors studied the action *in vitro* of aureomycin, circulin, and polymyxins B, D, and E on 7 strains of *Entamoeba histolytica* isolated from 7 patients. Amoebicidal activity was demonstrated at the following concentrations: aureomycin, 0·22 to 0·25 mg. per ml.; polymyxin B, 0·18 to 0·22; polymyxin D, 2·0 to 2·5; polymyxin E, 0·5 to 0·55, and circulin 2·25 to 2·50. At

these concentrations the concomitant bacteria survived. With each antibiotic a critical dilution was found at which the survival of the trophozoite, which was 7 to 8 days in control cultures, was prolonged to as many as 24 days. Two strains developed a slight increase in resistance to aureomycin, an initial sensitivity of 0·25 mg. per ml. rising to one of 0·45 mg. per ml. None of the strains developed resistance to polymyxins B and E. Polymyxin D and circulin, each of which was separately only weakly amoebicidal, had a synergistic effect in combination and became moderately amoebicidal.

Six patients were given 7 to 10 g. of aureomycin over a period of 4 to 5 days. Their stools became negative for *E. histolytica* after 3 days and remained negative for 20 to 25 days. *A. W. H. Foxell*

2178. **The Treatment of Amebiasis, with a Preliminary Report on the Use of Aureomycin**
C. F. GUTCH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 1407–1412, Dec., 1950. 11 refs.

Current amoebicidal drugs are reviewed and their limitations recognized. The danger of emetine is stressed: 13 out of 35 patients who had a normal electrocardiogram before receiving a course of 5 to 12 gr. (0·32 to 0·78 g.) of emetine showed abnormal tracings afterwards. Aureomycin was given orally in divided doses of 0·75 to 1 g. every 6 hours to a total of 28 g.

Macrophages and cellular debris disappeared from the stools, *x*-ray examination showed return of 4 cases of amoebic typhlitis to normal, symptoms rapidly improved, and all stools were negative at the end of course. The stools in 2 cases became positive in 6 weeks, but these responded to a second course, in 8 cases they remained negative for 5 months, and in 12 for 3 months. These results are contrasted with the 11·5% relapse rate recorded in combined treatment with emetine, carbarsone, and the iodine-containing oxyquinoline derivatives.

[To the abstracter these results appear too good to be true, even in these days of miracle drugs. Experience in Great Britain has not so far confirmed the opinion expressed elsewhere.] *Clement Chesterman*

OTHER INFECTIONS

2179. **Action of Deoxycortone Acetate on the Biochemical State of the Blood in Certain Infectious Diseases.** (Azione del desossicorticosterone acetato sullo stato biochimico del sangue in alcune malattie da infezione)
F. MULÉ, P. SEDATI, and L. GARUFI. *Pediatria* [*Pediatria*] **58**, 153–169, March–April, 1950. 29 refs.

The authors have investigated the effect of administration of deoxycortone acetate (DCA) on the colloidal dispersion of plasma proteins, the erythrocyte sedimentation rate (E.S.R.), and the oxidation of glutathione in 24 patients suffering from acute infectious diseases (8 with measles, 8 with scarlet fever, and 8 with typhoid fever). The experiments were carried out immediately after diagnosis and before giving any other treatment, the DCA being given by intramuscular or intravenous injection to the fasting patient. Blood examinations were carried out immediately before, and 2, 8, and 24 hours after, administration of the steroid.

For the study of the colloidal dispersion of the plasma protein a flocculation reaction suggested by one of the authors (Mulè, *Pediatria*, 1948, **56**, 1) was employed. The results are summarized in a table and indicate that the introduction of DCA into the blood modifies the isoelectric point of the plasma protein. This modification, which affects the flocculation of the plasma proteins, is related in degree to the dose of DCA employed and to the gravity of the disease, and is most evident after the injection of DCA by the intravenous route. The E.S.R. was determined by the Westergren method, readings being taken after half an hour, one hour, 4 hours, and 8 hours [only the one-hour readings being recorded in the paper]. Two hours after the administration of DCA there was a reduction in the E.S.R. in every case, but this improvement was not maintained, the rate after 24 hours having in almost every case returned to the figure obtained before the administration of the steroid. The blood glutathione level was estimated by the method of Woodward and Fry, readings being given in each case for the total glutathione, reduced glutathione, and oxidized glutathione levels. The results show an increase in the total glutathione (and in the proportion of reduced to oxidized glutathione) 2 hours after the administration of DCA in most cases. After 24 hours, however, the level had fallen below the initial figure in all but a few cases.

The authors conclude that in infectious diseases DCA (*a*) re-establishes the physiological balance of the blood chemical constituents, (*b*) detoxicates the milieu through the indirect action of glutathione, whose level in the blood increases after the introduction of DCA, and (*c*) re-establishes the enzymatic functional activity of the cells. *E. R. Cole*

2180. **Nervous Complications of Q Fever: Report of a Case with Symptoms of Mental Disturbance.** (Complicazioni nervose in corso di febbre Q: descrizione di un caso con sindrome amenziale)
R. FRASCARELLI. *Riforma Medica* [*Rif. med.*] **64**, 1333–1335, Dec. 9, 1950, 10 refs.

A somewhat emotional married woman of 40, menopausal and subject to headaches, became suddenly ill with fever, headache, generalized pains, and delirium, accompanied by vomiting, retention of urine and faeces, and a tendency to collapse. Penicillin and streptomycin were given without improvement and the patient was admitted to hospital in Perugia, where a diagnosis of Q fever was made on the finding of patchy consolidation at the base of the right lung. There were no neurological signs and the cerebrospinal fluid was normal. With aureomycin the temperature settled rapidly and the physical symptoms improved, but the patient became more confused and delirious, with facile episodes of singing and laughing and attempts at getting out of bed. She became difficult to control and especially to feed, and on the 26th day of her illness was transferred to a mental hospital. Here three applications of shock therapy were given and the patient slowly recovered, so that a fortnight

later she was able to leave the hospital symptom-free, but with almost complete amnesia for her illness.

The titre of complement-fixing antibodies for *Rickettsia burnetii* was 1 in 16 on the 9th day of her illness and had risen to 1 in 1,024 on the 22nd day.

Involvement of the nervous system in Q fever is not unknown and various psychoses have been noted; encephalitis with extrapyramidal signs, hemiplegia, facial palsy, and brachial neuritis are also recorded. The author is at a loss to explain their pathogenesis, but suggests the importance, in the present case, of the " soil " —an emotionally unstable, menopausal woman. He discounts the theory of activation of a neurotropic virus, believing the syndrome to be due to the action of *R. burnetii* itself—possibly an organism which has undergone mutation. *A. Paton*

See also Section Microbiology, Abstract 1917 (*a*), *b*), (*c*), and (*d*).

2181. **Pulmonary Histoplasmosis**
P. G. ARBLASTER. *Thorax* [*Thorax*] **5**, 333–339, Dec., 1950. 3 figs., 33 refs.

Human infection by the fungus *Histoplasma capsulatum* is reviewed, with particular attention to the syndrome of pulmonary calcification with a positive intradermal response to histoplasmin. Insensitivity to tuberculin is of aid in the diagnosis, but is not essential. This insensitivity is not due to a state of anergy, because following an injection of B.C.G. sensitivity develops. The author describes a patient who was under observation for 10 years and had the unique presenting symptom of haemoptysis. For 6 years the patient lived in Canada between Montreal and the Great Lakes. In 1938 he joined the British Army. In that year he had his first haemoptysis. He was thought to be suffering from pulmonary tuberculosis and was discharged from the Army. He remained well till 1945, when he had haemoptysis again and recovered; then in 1949, when he came under the author's care, he had a severe haemoptysis requiring blood transfusion. A chest radiograph revealed the characteristics of histoplasmosis: nodular calcified lesions with " halo-calcification " and gross mediastinal abnormalities. Comparison with radiographs taken in 1940 showed a progressive increase of calcium. The sputum was persistently negative on examination for tubercle bacilli, but a positive response to intradermal old tuberculin was produced. A systolic murmur was heard over most of the posterior surface of the right chest. There was, however, normal oxygen saturation in blood from the right brachial artery and so pulmonary arteriovenous anastomoses seemed unlikely. A fungus infection was thought the most likely diagnosis. An injection of coccidioidin 1 : 10 was negative, but 0·1 ml. at 1 : 10 dilution of standard histoplasmin produced a severe reaction locally. This was repeated 4 months later at a dilution of 1 : 1,000 and was again positive. Complement-fixing antibodies, which occur sometimes in histoplasmosis, were estimated, but the results were not significant. Collodion particles with adsorbed histoplasmin were not agglutinated by the patient's serum, and attempted cultures of the fungus from sputum and stools failed. A sternal-marrow smear was also negative for *Histoplasma capsulatum*, as might be expected from the duration of the disease. The criteria of diagnosis are discussed with reference to the histoplasmin test, the complement-fixation test, and the radiographic appearances.

The diagnosis of histoplasmosis in Britain is rare. In this case (as in the others reported) the probability is that infection occurred abroad, in Canada, and its progress was able to be observed over a 10-year period through the mistaken diagnosis of pulmonary tuberculosis. *Ronald S. McNeill*

2182. **A Probable Case of Pulmonary Histoplasmosis diagnosed in England**
J. CROFTON. *Thorax* [*Thorax*] **5**, 340–342, Dec., 1950. 2 figs.

In this case a radiograph of the chest was taken for the symptoms of mild chronic bronchitis. Calcified foci, 2 to 3 mm. in diameter, scattered throughout both lung fields were seen and at first glance suggested tuberculosis, but the wide dissemination and symmetry of the lesions caused second thoughts. Histoplasmosis was suspected and the patient revealed that 30 years previously he had been in Ontario, Canada, and had visited Detroit twice. Intradermal tests with 0·1 ml. of coccidioidin 1 : 1,000 and histoplasmin 1 : 1,000 and 1 : 100 showed positive reactions with the last two. Together with the unusual *x*-ray findings and the residence in an endemic area, this was considered sufficient evidence for a probable diagnosis of histoplasmosis.

A short description is also given of a second case with very similar findings which was discovered in a man aged 41 admitted to hospital with lobar pneumonia. He had travelled widely in central and southern U.S.A. *Ronald S. McNeill*

2183. **Subclinical Histoplasmosis. Gastro-intestinal Histoplasmosis of Children**
A. RAFTERY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **164**, 216–219, Jan. 27, 1951. 5 figs., 28 refs.

2184. **Clinical Studies in Human Strongyloidiasis. I. Semeiology**
C. A. JONES. *Gastroenterology* [*Gastroenterology*] **16**, 743–756, Dec., 1950. 2 figs., 12 refs.

This is a laborious study of the symptoms complained of by 100 patients in whom the larvae of *Strongyloides stercoralis* had been found on microscopical examination of the faeces and duodenal contents. [Many of the patients had other diseases more likely to cause their symptoms than strongyloidiasis.] Upper abdominal pain, nausea, vomiting and attacks of diarrhoea, were the commonest symptoms. *X*-ray examination showed deformity of the duodenal cap in 27 out of 36 patients with this syndrome. Of the total of 100 patients, 27 were classed as psychoneurotic. Eosinophilia was the most constant feature of the blood picture in these patients.

[Unfortunately the author gives no information as to the incidence of strongyloid infection in those without symptoms, and he does not state by what method the cases described were selected for study. Consequently the reader of this paper has to consider a number of facts the significance of which he is unable to determine.]

J, Naish

2185. **Clinical Investigations on the Chemotherapeutic Treatment of Urinary Bilharziasis. Part I. Intravenous Trivalent Sodium Antimony Gluconate**

J. M. WATSON and G. PRINGLE. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **53**, 233–238, Dec., 1950. 1 fig., 7 refs.

Tervalent sodium antimony gluconate was given to 5 patients suffering from urinary bilharziasis: 3 ml. of a freshly-prepared 6% solution in ice-cold, sterile, distilled water was given intravenously in the morning of 6 successive days. Each patient therefore received 18 ml., which contained 408 mg. tervalent antimony. The patients' weights ranged from 51 to 73 kg., the total dosage being 5 to 8 mg. per kg. of body weight. Reactions were slight: there was a slight evening fever after the first injections only: 2 patients showed no other reaction, but 3 complained of anorexia and one of these vomited twice.

Results of treatment were highly satisfactory. Haematuria rapidly disappeared and all patients had ceased to pass viable ova within one week of the completion of treatment. There were no relapses during the follow-up period of 3 months. The authors compare the drug favourably with other tervalent antimonials, where over 500 mg. of antimony seem necessary for cure, though the series is too small for exact comparison.

W. H. Horner Andrews

2186. **Reiter's Syndrome: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone**

M. A. OGRYZLO and W. GRAHAM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1239–1243, Dec. 9, 1950. 2 figs., 12 refs.

Since Reiter's description (in 1916) of the syndrome which bears his name, its boundaries have remained ill-defined, with emphasis on the triad of urethritis, conjunctivitis, and arthritis. All but one of the cases reported hitherto have been in young adult males. The causation of the disease remains in doubt. Some workers have recovered pleuropneumonia-like organisms from the genito-urinary tract and joint fluid (though they were unable to reproduce the disease experimentally); others have suggested that the syndrome is similar to dysenteric polyarthritis with toxic manifestations.

The present authors describe the effect of pituitary adrenocorticotrophic hormone (ACTH) and cortisone on the syndrome in 3 cases, inert injections being given both before and after the above preparations, so that the patients were unaware of any change in treatment. The patients, whose case histories are given, were all males, aged 29, 35, and 24 respectively. The first patient was treated with ACTH in doses of 25 mg. given intramuscularly every 6 hours for 12 days; the second with 10 mg. 4-hourly for 14 days, and the third with 25 mg. 6-hourly for 14 days. Response to ACTH was dramatic (within a few days) and relapse occurred 14 to 48 hours after discontinuing the treatment. In the third case 8 days after withdrawal of ACTH cortisone acetate was given intramuscularly in a dosage of 300 mg. daily for 3 days, 200 mg. for 10 days, and 150 mg. daily for 10 days, making a total of 4·4 g. The condition improved even more readily than with ACTH, and the subsequent relapse on withdrawal was not so severe. A few weeks later cortisone was given by mouth at 12-hourly intervals, the dosage being 300 mg. daily for 3 days, 200 mg. daily for 10 days, and 150 mg. daily for 4 days, making a total of 3·5 g.; it was as effective as when given by injection and the relapse seemed even milder. Clinical impressions were fully supported by laboratory tests. The authors point to one significant and satisfactory feature. In spite of relapse on withdrawal of treatment, the course of the disease was materially shortened in the first 2 cases (in which the patients recovered completely) and probably shortened in the third.

[A case which presented all the signs and symptoms of Reiter's syndrome (the only unusual feature being that the patient was a young woman) was demonstrated at the January (1951) meeting of the Heberden Society; cortisone administration was without effect, the disease actually progressing while it was being given.]

D. Preiskel

2187. **Oral Penicillin in the Prophylaxis of Recurrent Rheumatic Fever**

M. M. MALINER. *Journal of Pediatrics* [*J. Pediat.*] **37**, 858–861, Dec., 1950. 7 refs.

The author describes the use of troches containing 5,000 units of penicillin in a small group of children with rheumatism (63) or with congenital heart disease (23). Of the former 33 and of the latter 13 were given penicillin troches to suck 3 times daily from September to June, the remainder acting as controls. The bacteriological results are given with such conciseness that they are difficult to comprehend. It would seem, however, that β-haemolytic streptococci were infrequently present, whereas *Staphylococcus aureus* was isolated from "95% of all the cultures taken". In the control group there were two recurrences and in the treated group none. The author concludes [somewhat naïvely] that "this study confirms a previous opinion that 5,000 unit penicillin throat troches are of value in temporarily eliminating *S. haemolyticus* from the throats of rheumatic children". The condition of the staphylococci in regard to their resistance to penicillin before, during, and after the treatment does not appear to have been studied.

[This paper has no value as a contribution to the study of the prevention of recurrences of rheumatic fever.]

T. Anderson

2188. **Erythema Nodosum as Initial Manifestation of Boeck's Sarcoidosis**

F. E. CRAWLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1362–1364, Dec. 16, 1950. 3 figs., 9 refs.

History of Medicine

2189. **Surgeon General James Pierce, R.N.**
D. STEWART. *Journal of the Royal Naval Medical Service* [*J. R. nav. med. Serv.*] **36**, 214–225, Oct., 1950. 46 refs.

James Pierce, who, although the first head of the Royal Naval Medical Service, has previously received no recognition from naval medical historians, was a close friend of Samuel Pepys, who makes frequent reference in his diary to the intimate social connexions between his own and Pierce's family. They had much in common, both coming from the middle class of society and both beginning their careers as Commonwealth men and turning to the Stuarts at the Restoration. They worked for Charles II with great integrity and zeal and subsequently afforded similar loyal service to his brother James II, their careers terminating abruptly on the latter's abdication.

After having served for a time as a Surgeon in the Commonwealth Navy, Pierce became closely connected with the Court after the Restoration and, on the outbreak of war with the Dutch, was appointed Surgeon General of the Fleet by the Duke of York (later James II), High Admiral of England, and held this office from 1665 until 1689. A Surgeon General of the Fleet was appointed only in time of war and was responsible for the care of the sick and wounded only at sea, their care after disembarkation being the responsibility of the Commissioners of the Sick and Wounded. The examination and recruitment of naval surgeons was the duty of the Master and Wardens of the Company of Barber Surgeons, and each surgeon provided his own drugs and equipment, which were checked by authorities other than the Surgeon General. The Surgeon General of the Army, on the other hand, was more favourably placed both as to his powers and security of tenure of office, for he held a commission directly from the King and was also responsible for all appointments of army surgeons and for medical supplies. But by 1665 Pierce had become a Warden of the Company of Barber Surgeons and was taking a keen interest in the appointment of surgeons, while his correspondence with Pepys shows that he was actively concerned in the matter of their allowances. When the Fleet was not at sea, as in 1665, the Surgeon General was not paid, but on this occasion Pierce, who had gradually been extending the scope of his office, petitioned the King for remuneration on the grounds that he was still treating the sick and wounded and doing much routine administrative work, as well as looking after the financial interests of ships' surgeons and their widows. He was granted £100 per annum.

On the outbreak of the Third Dutch War in 1672 Pierce sailed in the flagship "Prince" and his earlier experience enabled him to make detailed arrangements for the comfort of the sick and wounded. He submitted a list of personnel, equipment, and stores necessary for the hospital ships, suitable diet schemes for the sick of all ships were drawn up, and bills were sent to the Barber Surgeons Company to authorize them to appoint surgeons to the Fleet. Pierce now also concerned himself with the surgeons' equipment and drugs, which were provided by each surgeon from a grant and were often of inferior quality. This long-standing scandal Pierce attempted to reform by suggesting that surgeons should obtain their drugs from a small number of reputable apothecaries. The proposal was abortive, but later the problem was solved by the authorization of the Society of Apothecaries to supply drugs to the Navy. [The provision of drugs for the armed services at this time was far in advance of the practice under the civil public service, Poor Law doctors having to supply their own drugs until late into the nineteenth century.]

In 1680 Pierce combined the work of Surgeon General to the Army with his naval appointment, was in charge of the disposal of the sick during the Tangiers and Sedgemoor operations, and was responsible for the planning of a military hospital at Hounslow. His career ended in 1689 when he was suspected of intriguing against the new regime of William III and, although nothing was proved against him, he lost his various offices.

Ruth Hodgkinson

2190. **Henry Bence Jones**
H. N. SEGALL. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 605–609, Dec., 1950. 10 refs.

Henry Bence Jones is remembered for the "Bence-Jones bodies" found in the urine of patients suffering from multiple myeloma. He came of Irish stock, being the second son of Colonel William Jones of the Dragoon Guards, and was born at Thorington Hall, Yoxford, Suffolk, on December 31, 1813*. He was educated at Harrow and Cambridge (Trinity, B.A. 1836, M.A. 1842) whence he proceeded to St. George's Hospital in October, 1836. After becoming L.R.C.P. in 1841* he went to Giessen to study under Liebig, the founder of biochemistry. He began to practise in London in 1842, became physician to St. George's in 1845*, and F.R.C.P. in the same year.

Jones was a skilful physician with a great enthusiasm for the new science of "animal chemistry" and his chief aim was to base therapeutics on scientific principles. He was the author of nine books and forty scientific papers, the best known of which to-day is his paper "On a new substance occurring in the urine of a patient with mollities ossium", which was presented to the Royal Society on February 25, 1847, read on April 22, and published in the *Philosophical Transactions* in 1848 as well as in Liebig's *Annalen* of the same year.

The case was that of a man aged 47 who was attended by Dr. Macintyre and Dr. Watson and who died on January 2, 1846. Jones received a sample of the patient's

urine on November 1, 1845. The necropsy revealed the condition of the bones. Three reports of this case were published, the first (histological) by Dalrymple (*Dublin Quart. J. Med. Sc.*, 1846, **2**, 85), the second by Jones, already mentioned, and the third by Macintyre (*Med.-chir. Trans.*, 1850, **30**, 211).

Macintyre really deserves credit for the discovery of the so-called " Bence-Jones bodies ". The test we now use was originated by him and described in the note accompanying the specimen sent to Jones.

Bence Jones described his observations in great detail and even gave a chemical formula for the " coagulum " found in the urine. The recognition of its relation to multiple myeloma and its value in diagnosis developed very slowly. The first reported case in the United States of America was described by Fitz in 1898 (also the first to be confirmed by *x* rays) and this stimulated Osler to include it in the third edition of his text-book.

Bence Jones died at the age of 59 on April 20, 1873, from cardiac disease.

[* D.N.B. gives 1814, 1842 and 1849 respectively.]

F. N. L. Poynter

2191. **Professor Jules Fontan and the Naval Medicine of his Time.** (Le Professeur Jules Fontan et la médecine navale de son époque)
—. OUDART. *Revue de Médecine Navale* [*Rev. Méd. nav.*] **5**, 149–175, 1950. 1 ref.

2192. **René Descartes, 1596–1650. A Short Note on His Part in the History of Medicine**
H. P. BAYON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 783–785, Nov., 1950. 9 refs.

2193. **William Withering. Biographical Notes**
K. D. WILKINSON. *Queen's Medical Magazine* [*Queen's med. Mag.*] **43**, 127, Oct., 1950. 2 figs.

2194. **Richard Bright—a Bio-bibliography**
W. HILL. *Guy's Hospital Gazette* [*Guy's Hosp. Gaz.*] **64**, 393–397 and 472–484, Oct. 21 and Dec. 16, 1950. 1 fig.

2195. **William Henry Welch—April 8, 1850, to April 30, 1934**
W. R. BETT. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 847–850, Nov., 1950. 1 fig., 4 refs.

2196. **Conrad Gessner's Relations with a Croatian Scholar.** (Conrad Gessners Beziehungen zu einem kroatischen Gelehrten)
L. GLESINGER. *Gesnerus* [*Gesnerus*] **7**, 27–50, 1950. Bibliography.

2197. **The Significance of Korsakov's Work in the Development of Russian Psychiatry.** (Значение С. С. Корсакова в развитии отечественной психиатрии)
V. M. BAUTHCHIKOV. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 7–27, Sept.–Oct., 1950. Bibliography.

2198. **The Inheritance from Korsakov in Russian Psychiatry.** (Наследие С. С. Корсакова и советская психиатрия)
M. O. GUREVICH. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 27–30, Sept.–Oct., 1950. 3 refs.

2199. **Korsakov as a Man and as a Psychiatrist.** (С. С. Корсаков как человек и как врач-психиатр)
T. A. GEJER. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 31–32, Sept.–Oct., 1950.

2200. **Korsakov and Modern Psychiatry.** (С. С. Корсаков и практика современной психиатрии)
S. V. KRAJTS. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 32–34, Sept.–Oct., 1950.

2201. **Korsakov as Doctor and Scientist.** (С. С. Корсаков как врач и ученый)
A. GALACHJAN. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 34–38, Sept.–Oct., 1950. 11 refs.

2202. **The Catamnesis of a Case of Polyneuritic Psychosis, Diagnosed 50 Years Ago by Korsakov.** (Катамнез случая полиневритического психоза, диапносцированного 50 лет назад С. С. Корсаковым)
I. V. KATARINOVA. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 38–40, Sept.–Oct., 1950. 1 ref.

2203. **The History of Russian Neuropathology. (Russian Work on Jacksonian Epilepsy).** (К истории русской невропатологии (о корковой частичной эпилепсии))
J. M. TERNER. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 41–42, Sept.–Oct., 1950. 3 refs.

2204. **Fifty Years of Physiology**
K. J. FRANKLIN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 789–796, Nov., 1950. 1 fig., bibliography.

2205. **The History of Diverticulitis of the Intestine**
S. W. PATTERSON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **43**, 785–789, Nov., 1950. 43 refs.

2206. **Lithotomy in Women in Ancient Indian Medicine.** (Zum Blasensteinschnitt beim Weibe in der altindischen Medizin)
R. F. G. MÜLLER. *Zentralblatt für Gynäkologie* [*Zbl. Gynäk.*] **72**, 1441–1443, 1950. 9 refs.

2207. **Leonardo Bianchi and the Doctrine of Cerebral Localization.** (Leonardo Bianchi e la dottrina delle localizzazioni cerebrali)
O. FRAGNITO. *Rassegna Clinico-scientifica dell'Istituto Biochimico Italiano* [*Rass. clin.-sci. Ist. biochim. ital.*] **26**, 291–296, Oct., 1950.

2208. **Fifty Years of Medical Research in Australia**
E. V. KEOGH. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 24–28, Jan. 6, 1951. 2 figs.